The New England
Journal of Medicine

Copyright, 1942, by the Massachusetts Medical Society

VOLUME 227 NOVEMBER 5, 1942 NUMBER 19

TETANUS TOXOID IMMUNIZATION OF ADOLESCENTS*

Skin Reactivity, Allergy and Unfavorable Reactions

J. ROSWELL GALLAGHER, M.D.,† CONSTANCE D. GALLAGHER, B.A.,‡ AND GUSTAV G. KAUFMANN, M.D.§

ANDOVER, MASSACHUSETTS

PROPHYLAXIS against tetanus is of special interest to physicians who deal with adolescents. Members of that age group, because of their athletic and other activities, suffer frequent minor injuries, and the question of whether or not to give tetanus antitoxin prophylactically arises repeatedly; one must frequently choose between the dangers, discomforts and horse-serum sensitization of tetanus antitoxin and the possibility of tetanus following an apparently trivial wound. The present development of tetanus toxoid, reports of its efficiency in producing a protective level of antitoxin in the recipient's serum, and evidence that its administration is only rarely accompanied by unfavorable reactions appear to have solved, to a considerable extent, the problem of tetanus prophylaxis.

Inevitably, when the widespread use of a new prophylactic measure is suggested, attention becomes focused, and usually to an unreasonable extent, on the frequency and degree of unfavorable reactions produced by that agent. Hall,[1] in reporting the results of immunizing 2300 midshipmen, states that only 1 developed urticaria, only 2 had fever and malaise, and only 8 complained of sore arms after the first dose of alum precipitated tetanus toxoid; following the second dose, 1 case of anaphylactic shock, 4 cases of urticaria and 38 sore arms developed. During the following year, 793 men were immunized with a different preparation of toxoid, and an unfavorable reaction occurred in only 1 case. Whittingham,[2] in reporting the immunization of 61,000 men in the Royal Air Force, states that only 5 had malaise and fever and that 9 developed urticaria. A group of 186 allergic children, ranging from three to fifteen years of age, were immunized by Peshkin,[3] without any disturbing reactions: only 2 had a brief elevation in temperature.

The various objectionable features of tetanus antitoxin and the low incidence of unfavorable reactions from tetanus toxoid in such groups as those mentioned above, together with the apparent efficiency of toxoid in raising the serum antitoxin to a protective level, made us urge the parents of a group of adolescents under our care to have them actively immunized against tetanus. Extensive experience in the use of tetanus toxoid among adolescents is apparently lacking, and because of the frequency of unfavorable reactions from diphtheria toxoid in this age group, we approached our project more conservatively than the experience of others with different age groups seemed to justify.

Rogers[4] has emphasized the desirability of this immunization for all allergic children, in whom the reports of Peshkin[3] and Unger[5] indicate that unfavorable reactions are uncommon. However, recent orders from the War Department[6] suggest that allergic persons be skin tested and, if the skin test is positive, be given tetanus toxoid in divided doses; to be ultraconservative and also to determine the skin reactivity to toxoid in those persons both with and without an allergic history, we decided to test each boy in our series prior to each immunizing dose of tetanus toxoid. The results of these skin tests, the incidence of unfavorable reactions and the relations between these skin tests, reactions and various allergic states are reported.

METHOD

Permission to give tetanus toxoid was obtained from the parents of about 500 boys, who ranged in age from thirteen to nineteen years. Alum precipi-

*From the Department of Health, Phillips Academy.
This study was aided by a grant from the Carnegie Corporation.
†School physician, Phillips Academy.
‡Research associate, Phillips Academy.
§Assistant school physician, Phillips Academy.

tated toxoid in two doses of 1 cc. each was given; the interval between doses ranged from four to seven weeks. Prior to each dose, 0.1 cc. of a 1:10 physiologic saline dilution of the tetanus toxoid was injected intradermally, and after an interval of ten minutes, the skin reaction was recorded; in the rare cases in which the skin reaction was very strongly positive, the undiluted toxoid was given in divided doses — 0.1, 0.2, 0.3 and 0.4 cc. — on four successive days. The degree of "sore arm" and of malaise, as recorded, was based on questions directed to each boy, and was obviously greatly influenced by the boy's personality as well as by our interpretation of his statements.

Results

Table 1 presents the results of skin testing with a 1:10 physiologic saline dilution of tetanus toxoid that was injected intradermally before the first immunizing dose was administered. Eight per cent of the entire group showed a skin reaction measuring 10 mm. or more in diameter, and 3.7 per cent showed a strongly positive (++ or +++) reaction.

Table 1. *Results of Skin Tests before Tetanus Toxoid Immunization.*

Reaction	No. of Cases	Percentage of Total
Negative	373	73.3
Less than 10 mm. in diameter (±)	95	18.7
10 to 20 mm. (+)	22	4.3
20 to 30 mm. (++)	6	1.2
30 mm. or more (+++)	13	2.5
Total	509	

Table 2 lists the incidence of asthma, hay fever, previous tetanus antitoxin prophylaxis and hay fever or asthma prophylactic therapy in each group. The large percentage of boys who had been given tetanus antitoxin in the past is interesting, but the most significant fact is that about 36 per cent of the group that was strongly positive to the skin tests gave no history of previous tetanus-antitoxin prophylaxis or allergy and only 5 of the 19 who had strongly positive skin tests gave a history of asthma or hay fever. The fact that 23 per cent of the +++ reactors had asthma is worthy of attention, but this seems less significant in view of the large number of those with asthma who had negative skin tests. It is of interest that of the 10 students who regularly received some sort of allergy prophylaxis, only 1 had an initial skin test with diluted tetanus toxoid greater than 20 mm. in diameter.

Table 3 shows clearly that the highest percentage of students having a history of various allergic states or previous prophylaxis always fell in the group with negative skin tests and that only relatively small percentages of each of these had strongly positive reactions.

The changes in skin reactivity following the inoculation of the first 1-cc. dose of tetanus toxoid and measured just before the administration of the second prophylactic dose were recorded. The entire group was not given a second skin test, but no boy whose first test was positive was omitted. Negative skin tests were recorded at both times in 318 cases; 109 others had approximately the same degree of reaction at both the first and second skin tests. In 10 cases, the first skin test measured less than 20 mm., and the second test was recorded as negative; second tests were recorded as + in 10 subjects whose initial tests were negative. Three boys whose initial skin test was recorded as ++ had at their second test a ± reaction, and 9 whose initial skin test was ± had a skin test of ++ or +++ following their first immunizing dose of toxoid; in only these last 12 cases (2.6 per cent), was there a significant change in skin reactivity subsequent to the inoculation of an immunizing dose of tetanus toxoid. Of the 9 boys whose initial skin test was ± or negative and whose second test was ++ or +++, 1 had asthma, 5 had hay fever, and 2 of these and 1 other had been given tetanus antitoxin in the past; 2 of these 9 boys had neither

Table 2. *Incidence of Asthma, Hay Fever and Previous Tetanus and Allergy Prophylaxis according to Reactions.*

Reaction to Skin Test	Total No. of Cases	No History of Allergy or Previous Prophylaxis		History of Asthma		History of Hay Fever		Previous Tetanus Prophylaxis		Previous Allergy Prophylaxis	
		No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Negative	373	245	65.7	13	3.5	45	12.1	84	22.6	5	1.4
±	95	61	64.2	3	3.1	21	22.1	18	18.9	3	3.1
+	22	14	63.7	2	9.1	2	9.1	6	27.3	1	4.5
++	6	2	33.3	0	0	0	0	4	66.7	0	0
+++	13	5	38.4	3	23.1	2	15.4	3	23.1	1	7.7
Totals	509*	327		21		70		115		10	

*The total number of cases (509) does not correspond to the total number of histories (543) since many of the boys were classified in more than one group.

an allergic history nor a previous dose of tetanus antitoxin. Fifteen boys were given tetanus toxoid in divided doses on the basis of strongly positive skin reactions; in 11, the initial and second skin tests were approximately the same; in 4, the skin reactivity at the time of the second test was recorded as +.

Table 4 shows that only about 16 per cent of the boys who had strongly positive skin tests complained of very sore arms or any malaise after the first dose of toxoid, and that a moderate number of those who had similar complaints had negative skin tests.

Table 4. *Incidence of Effects following Both the First and Second Immunizing Doses of Toxoid according to the Degree of Skin Reactivity before the First Dose.*

Effect	Total No. of Cases	No. of Cases				
		−	±	+	++	+++
Sore arms						
Slight	64	48	12	0	0	4*
Moderate	27	14	6	3	1	3*
Malaise						
Slight	17	13	0	1	0	3*
Moderate	2	1	1	0	0	0
Admitted to infirmary	12	9	3	0	0	0
After first dose	4	4	0	0	0	0
After second dose	8	5	3	0	0	0
Sterile abscess†	2	2	0	0	0	0*
Urticaria‡	1	0	0	0	0	1§
Anaphylactic reaction	0	0	0	0	0	0

*Two boys in this group were given toxoid in divided doses.
†After each dose.
‡Urticaria also following the second skin test; second immunizing dose not given.
§This boy was given toxoid in divided doses.

Of the 12 boys admitted to the infirmary because of headache, malaise and fever, all of about twenty-four hours' duration, none had a positive skin test. Two boys, whose skin tests were negative, developed sterile abscesses at the site of injection a few days following both the first and second inoculations. Another, whose skin tests were strongly positive, developed giant urticaria after his first inoculation, given in divided doses; the second skin test was followed within four hours by the development of giant urticaria (which responded to adrenalin), and the second immunizing dose was omitted. No anaphylactic reactions occurred: 3 boys "felt faint" directly following their inoculations, but their apprehension and pallor before inoculation indicated that these reactions were psychogenic.

Table 3. *Incidence of Reactions according to History.*

History	Total No. of Histories	−		±		+		++		+++	
		No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage
No history of allergy or previous prophylaxis	327	245	74.9	61	18.7	14	4.3	2	0.6	5	1.5
History of asthma	21	13	61.9	3	14.3	2	9.5	0	–	3	14.3
History of hay fever	70	45	64.2	21	30.0	2	2.9	0	–	2	2.9
Previous tetanus prophylaxis	115	84	73.0	18	15.7	6	5.2	4	3.5	3	2.6
Previous allergy prophylaxis	10	5	50.0	3	30.0	1	10.0	0	–	1	10.0
Totals	543	392		106		25		6		14	

Table 5 presents the incidence of unfavorable reactions among boys with a history of hay fever or asthma, or both, as compared with the reactions in those without history of allergy. It is obvious that there was no striking difference in the incidence of reactions in the two groups.

Discussion

Our experience and that of many others clearly indicate that immunization with tetanus toxoid is a practical, safe and very desirable procedure; immunization at an early age and in combination with diphtheria antitoxin appears to be the method of choice, but our results indicate that the use of tetanus toxoid is satisfactory during adolescence.

The relatively high incidence of unfavorable reactions from diphtheria toxoid during adolescence and our belief that results obtained in other age groups should not be applied without careful investigation to adolescents were factors that interested us in the skin reactivity of this group to diluted tetanus toxoid. Because of the hesitancy of some physicians to give this prophylaxis to allergic persons, who obviously need it most, and because of recent War Department orders to proceed with caution in the immunization of all allergic persons, it is interesting that skin sensitivity to diluted tetanus toxoid is far from limited to members of the group having a history of allergy, and that although about 38 per cent of those having strongly positive skin tests had either asthma or hay fever, only about 14 per cent of those with asthma had strongly positive skin tests. Local and systemic reactions were no more frequent among those with positive skin tests to tetanus toxoid than among those who did not exhibit such sensitivity, but these results may have been affected by our procedure in giving divided doses to strongly positive subjects. A significant number (36 per cent) of boys with strongly positive skin tests gave no allergic history, and a considerable

number of those who had unfavorable reactions had both a negative skin test and a negative allergic history; it appears that neither skin reactivity to tetanus toxoid nor history of previous allergic manifestations is a reliable indicator of the possibility of local or systemic reaction. Fortunately, no anaphylactic reactions were encountered in this group; one can only speculate whether anaphylactic or other reactions might have developed in any of the 15 boys whose skin tests were strongly positive had they been given full instead of divided doses of tetanus toxoid, but we do know that unfavorable reactions were negligible, except for 1 case of urticaria in this group. Four boys who had ++ skin tests were given full doses of toxoid: none of them had immediate unfavorable reactions, and none subsequently complained of sore arms or required admission to the infirmary, and only one complained of slight malaise. It seems necessary, before either the value of skin testing or the desirability of giving small divided doses to persons positive to the skin test can be determined, to investigate further the relation of anaphylactic or other severe reactions to skin sensitivity to toxoid and the incidence of severe reactions in strongly positive tests when toxoid is administered in full rather than divided doses. On the basis of our experience, the conservative and safe procedure in immunizing members of the adolescent age group is to precede the inoculation of tetanus toxoid by a skin test; little time or effort can be lost by this procedure, and until a more extensive experience with adolescents is available, conservatism is certainly commendable. Our results indicate that in only a small number of cases did initial mild skin reactions change to more strongly positive ones following the administration of the first dose of toxoid, and unless one is to be ultraconservative, a skin test prior to the second immunizing dose is hardly indicated.

Table 5. *Comparison of Unfavorable Reactions Occurring in Boys with and without a History of Allergy.*

	Total No. of Cases	Sore Arms		Malaise		Infirmary Admission		Abscess	Urticaria
		No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage	No. of Cases	No. of Cases
History of allergy	75	16	21.3	3	4.0	2	2.7	0	0
No history of allergy	434	75	17.0	16	3.7	10	2.3	2	1
Totals	509	91		19		12		2	1

Strongly positive skin tests to diluted tetanus toxoid were recorded in 3.7 per cent of the group; 1 case of urticaria occurred, 2 sterile abscesses developed, and 12 subjects had sufficient malaise and fever to warrant infirmary care for twenty-four hours.

There is apparently little relation between known previous allergic states and skin sensitivity to diluted tetanus toxoid.

Neither skin sensitivity to diluted tetanus toxoid nor elicited previous history of allergic manifestations was found to be a reliable criterion on which to predict skin sensitivity or the development of unfavorable local or systemic reactions.

Fifteen of the 19 boys whose skin tests were strongly positive were given toxoid in four divided doses; no unfavorable reactions occurred in this group.

Until further experience with this age group is evaluated, it is suggested that skin tests with diluted tetanus toxoid be made prior to the administration of each immunizing dose.

Summary

Five hundred and nine boys ranging from thirteen to nineteen years of age were given two immunizing doses of tetanus toxoid without subsequent development of serious local or systemic reactions; the incidence of unfavorable reactions, however, was apparently higher in this group than among either younger or older subjects.

References

1. Hall, W. W. Tetanus toxoid immunization in the United States Navy. *Ann. Int. Med.* 14:565-582, 1940.
2. Whittingham, H. E. Anaphylaxis following administration of tetanus toxoid. *Brit. M. J.* 1:292, 1940.
3. Peshkin, M. M. Immunity to tetanus induced by combined alum-precipitated diphtheria and tetanus toxoids, based on study of 186 allergic children. *Am. J. Dis. Child.* 62:9-25, 1941.
4. Rogers, R. P. The use of tetanus toxoid in private practice. *Bull. New York Acad. Med.* 15:553-559, 1939.
5. Unger, L. Tetanus toxoid in the prevention of tetanus and serum reactions in allergic persons. *J. Allergy* 13:135-138, 1942.
6. Circular letter: No. 110, November 10, 1941. War Department: Office of the Surgeon General, Washington, D. C.

ADEQUATE CLINICAL RECORDS — A PROFESSIONAL RESPONSIBILITY*

JOSEPH H. PRATT, M.D.†

BOSTON

IT is a fact as remarkable as it is disturbing that physicians on the whole do not realize the value of medical records of the patients under their care. This neglect is all the more surprising because leading medical teachers have by precept and example emphasized the value of the clinical history and of careful observations made at the bedside. The injunction to observe, to record and to analyze has often been made. It is necessary to have as good medical records in a small hospital as in a large one because the patient presents the same problems in each: he is entitled to thorough study and his record should be written promptly, accurately and completely.

Dr. Malcolm T. MacEachern,[1] director of hospital activities of the American College of Surgeons, states: "Prior to the commencement of the hospital standardization program in 1918, only a limited number of hospitals in the United States, less than one hundred, kept medical records of an acceptable type. The remainder of the hospitals had scant information other than that found in the nurses' notes." The minimum standard established twenty-four years ago by the American College of Surgeons and efforts to secure its enforcement have resulted in some improvement, but much remains to be done. Clause 4 of the minimum standard relates to medical records; it states, "that accurate and complete records be written for all patients and filed in an accessible manner in the hospital. . . ." It defines a complete medical record as one that includes identification data, complaint, personal and family history, history of the present illness, physical examination, special examinations, provisional or working diagnosis, medical or surgical treatment, gross and microscopic pathological findings, progress notes, final diagnosis, condition on discharge, follow-up and, in fatal cases, autopsy findings. Unfortunately, many hospitals — even some of those approved by the American College of Surgeons — keep records that are far from satisfactory. The fault lies in the failure of the members of the medical staff of the hospital to become "record conscious." Much of the blame can be traced back to the clinical teachers in the medical schools, who did not instill into the minds of their students the necessity of keeping detailed records if they are to do justice to themselves or to their patients.

Hippocrates,[2] in the dawn of history, recorded as accurate observations as were possible at that time and made daily progress notes in acute cases. An example, selected almost at random, is Case 4 from the 26 cases he collected for his third book on epidemics:

> In Thasus, Philistes had headache of long continuance, and sometimes was confined to bed with a tendency to deep sleep; having been seized with continual fevers from drinking, the pain was exacerbated; during the night he at first became hot. On the first day he vomited some bilious matter, at first yellow, but afterwards of a verdigris-green color and in greater quantity; formed feces passed from the bowels; passed the night uncomfortably. On the second day, deafness, acute fever, retraction of the right hypochondrium; urine thin, transparent. . . . On the third in an uncomfortable state. On the fourth, convulsions. All the symptoms exacerbated. On the fifth early in the morning, died.

This record presents clearly and objectively, four hundred years before the birth of Christ, what appears to be a fulminating case of meningitis. There is great need today of cultivating this ancient diligence of Hippocrates in the recording of medical cases.

Laënnec, the greatest name in medicine after Hippocrates, based his epoch-making work in auscultation on his records of detailed physical findings and his autopsy notes in diseases of the chest.

As an illustration of how bad records are today, I cite the following recent experience. I saw a patient on the eighth day of her illness and made the following note:

> *February 17, 1942*: Mrs. S. K., aged 31. Complains of frequent chills and fever.
>
> *Present Illness*: Came down with a sore throat on February 10. The next day cough began and she had a tight feeling behind the sternum. On the night of February 12, she awoke feeling very hot; she took her temperature and found it to be 102.5°F. Doctor called the morning of February 13; examination of the chest was negative, but the temperature was not taken. The patient raised much greenish sputum on the following day; previously, the cough had been dry. She had a series of shaking chills lasting half an hour or so beginning on the night of February 14, followed by a sense of great heat. On February 15, the temperature reached 101.5°F. Yesterday morning about 7 o'clock, it was 100°F. At 11:30, it was 98.6°F. At about 4 p.m., the temperature was 103.5°F. A shaking chill occurred in the middle of the night.

Examination of the chest was negative. Although the oral temperature at the time of examination

*Read at the twentieth meeting of the New England Hospital Assembly, Boston, March 11, 1942.

†Professor of clinical medicine, Tufts College Medical School; physician-in-chief, New England Medical Center.

was 101.1°F., the respirations were only 16. There was no leukocytosis, and the urine was normal. It was evident that this was an unusual case that demanded careful study for a correct diagnosis. The patient was sent to an excellent small hospital in a neighboring town where resident physicians, a full-time roentgenologist and a pathologist were on the staff.

The history of the present illness, taken by a salaried resident physician, was as follows: "*Chief Complaint*: Chills and fever. Burning on urination. Date of onset week today, which began as a heavy chest cold." No attempt at a record would have been better because two of the three statements made were false and hence misleading: the patient had had no burning on urination, and she had not had a chest cold.

FIGURE 1.

On inquiry, I found that there was no supervision of this resident's records. The history as I have given it stands as the official record. The case history as given by me was typical of virus pneumonia, a disease that has only recently been recognized and presents a striking and characteristic clinical picture. This was subsequently proved to be the correct diagnosis. The resident, of course, learned nothing from his so-called "study" of the case. Because this history was the worst I think I have ever read in my experience of forty-seven years, I interviewed the young man and found that he had graduated from an unrecognized school, where he had had no practical instruction or experience in case taking. He had served an internship in a large hospital, where he had had a large experience in case taking, but his clinical histories had been accepted without correction and his records had never been supervised by the attending physicians.

A pleasing contrast to the unsatisfactory state of medical records in many hospitals of New England today is presented by an examination of the medical records of the Massachusetts General Hospital made over a hundred years ago (Fig. 1).

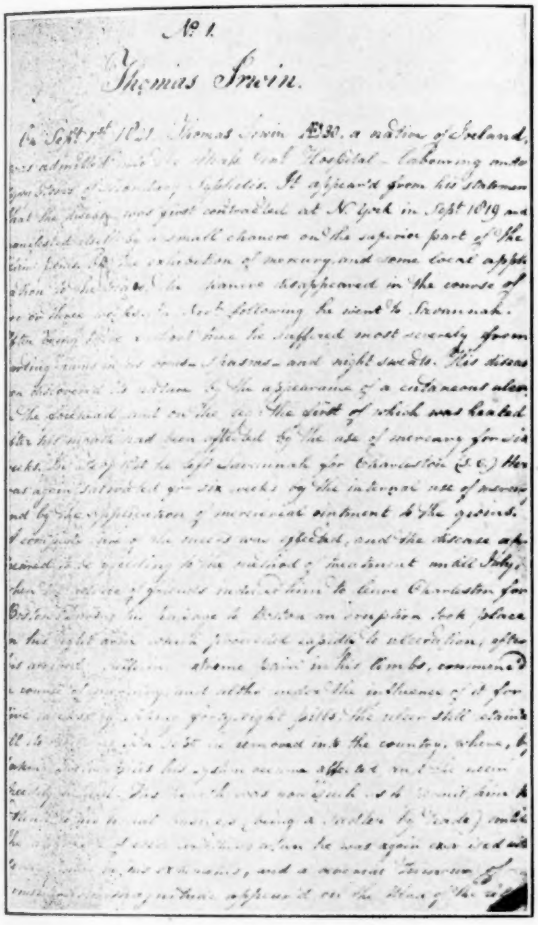
This hospital was opened in September, 1821. Since that date, the records have been carefully preserved. The first 50 cases were bound to form Volume 1 of the medical records. For about a hundred years thereafter, each series of 50 cases was bound in a separate volume. These early case reports are worthy of study. The history of the very first case was written out in detail (Fig. 2). The careful penmanship attests to the value attached to the clinical record. I have read that the physician's notes were copied for the official record by the hospital apothecary, who wrote a fine hand. James Jackson was the physician-in-chief. His opinion of the worth of medical records is attested by his own statement:

> It has been the practice at the Massachusetts General Hospital, in the medical department, to note the state of the patient every day, in acute cases, as our records show. It has been our intention to inquire into the state of all the functions in the beginning of each case, and more or less fully from day to day. But we have been willing to diminish the labor of our records by mentioning only the functions which manifested disease, while oftentimes we made no records of those which appeared healthy. Unless it was certain, however, that this course was uniformly pursued, it is obvious that there must be some uncertainty in any given case, whether something had not been omitted. There is no doubt that our negligences have been so frequent that our records cannot be relied on, except for what is positively stated. Nor can we say that our inquiries have been sufficiently full originally. We have often failed in learning and still oftener in stating the previous histories of our patients. . . . In the first years we were the most deficient, but we have made our observations with more and more care as we have proceeded.

He wrote these words in his classic report on typhoid fever,[3] communicated to the Massachusetts Medical Society in 1838.

Where did Dr. Jackson get his conviction of the significance of hospital records, which possessed

him when he first took charge of the medical work at the hospital in 1821? Doubtless, the answer is, From his teachers in Great Britain, where he "walked" the hospitals of London and Edinburgh in 1800. It seems evident that the case records of these British hospitals must have been good and



No 1.

Thomas Irwin.

FIGURE 2.

that he took them as a model when the Massachusetts General Hospital was opened. Additional evidence of the importance attached by Scottish hospital physicians to clinical records in the first half of the last century was the custom, introduced by them, of giving the name of the clinical clerk who made the record when they published the notes of the case in a medical paper.

It is of interest to discover and give credit to the physician who first taught and practiced the approved modern plan of making and recording a thorough clinical history and complete physical examination. I am convinced from my reading that this honor belongs to the great French physician, Pierre Charles Alexander Louis. In addition to a careful history of the family, the past diseases and the present illness, we have the testimony of James Jackson[4] that Louis made and recorded more thorough observations than any of his predecessors:

> He noted the actual phenomena present at his examination, depending for this not only on the statement of the patient, but on his own senses, his eyes, his ears, and his hands . . . he was not satisfied with noting the functions, in which the patient complained of disorder, but examined carefully as to all the functions; recording their state as being healthy or otherwise, and even noticing the absence of symptoms which might bear on the diagnosis.

I have heard Osler refer to Louis as the patron saint of the Massachusetts General Hospital, but it was not the influence of Louis that first led James Jackson to keep good records from the opening of the hospital. This is a known fact, since Jackson has left on record the statement that he first learned of Louis's work in 1830. This was nine years after the opening of the hospital. His later debt to Louis, he freely acknowledged. The value of making and recording the physical examination in the manner outlined above, was taught him by Louis. In the first case admitted to the hospital, there was not a single entry on the objective symptoms and signs presented by the patient at the time of his entry, the record dealing solely with the present and past history. This defect was soon remedied, and it was not long before careful notes were made of the objective findings.

In the summer of 1833, James Jackson, Jr., then twenty-three years of age, returned to Boston after nearly two years of study in Paris, carried on chiefly under the direction of Louis. On the morning of October 15, 1833, young Jackson went to the Massachusetts General Hospital, where he examined a patient ill with typhoid fever, who had been admitted on the previous evening to his father's service, and recorded the following notes on the case (I give them in full as they furnish convincing evidence that the quality of this medical record, made one hundred and eight years ago, and the care and thoroughness of the observations were of a high order):

> October 15, 1833 — S. K., aet. 32, unmarried, eyes, hair and complexion dark; maid-servant; born in Salem. Entered the hospital last evening. Ill since seventh instant, perfectly well before; on that day headache, distress and pain in limbs, anorexy, weakness, obliging her to go to bed. Since then she has had bad taste in mouth; no soreness of throat, nor dysphagia; thirst; anorexy; nausea after taking too much liquid, but not at other times; diarrhoea from the first, four or five dejections a day; urine not observed; catamenia on 10th, lasting one day (they had occurred in order the week preceding); no chills; occasional

was 101.1°F., the respirations were only 16. There was no leukocytosis, and the urine was normal. It was evident that this was an unusual case that demanded careful study for a correct diagnosis. The patient was sent to an excellent small hospital in a neighboring town where resident physicians, a full-time roentgenologist and a pathologist were on the staff.

The history of the present illness, taken by a salaried resident physician, was as follows: "*Chief Complaint*: Chills and fever. Burning on urination. Date of onset week today, which began as a heavy chest cold." No attempt at a record would have been better because two of the three statements made were false and hence misleading: the patient had had no burning on urination, and she had not had a chest cold.

FIGURE 1.

On inquiry, I found that there was no supervision of this resident's records. The history as I have given it stands as the official record. The case history as given by me was typical of virus pneumonia, a disease that has only recently been recognized and presents a striking and characteristic clinical picture. This was subsequently proved to be the correct diagnosis. The resident, of course, learned nothing from his so-called "study" of the case. Because this history was the worst I think I have ever read in my experience of forty-seven years, I interviewed the young man and found that he had graduated from an unrecognized school, where he had had no practical instruction or experience in case taking. He had served an internship in a large hospital, where he had had a large experience in case taking, but his clinical histories had been accepted without correction and his records had never been supervised by the attending physicians.

A pleasing contrast to the unsatisfactory state of medical records in many hospitals of New England today is presented by an examination of the medical records of the Massachusetts General Hospital made over a hundred years ago (Fig. 1).

This hospital was opened in September, 1821. Since that date, the records have been carefully preserved. The first 50 cases were bound to form Volume 1 of the medical records. For about a hundred years thereafter, each series of 50 cases was bound in a separate volume. These early case reports are worthy of study. The history of the very first case was written out in detail (Fig. 2). The careful penmanship attests to the value attached to the clinical record. I have read that the physician's notes were copied for the official record by the hospital apothecary, who wrote a fine hand. James Jackson was the physician-in-chief. His opinion of the worth of medical records is attested by his own statement:

> It has been the practice at the Massachusetts General Hospital, in the medical department, to note the state of the patient every day, in acute cases, as our records show. It has been our intention to inquire into the state of all the functions in the beginning of each case, and more or less fully from day to day. But we have been willing to diminish the labor of our records by mentioning only the functions which manifested disease, while oftentimes we made no records of those which appeared healthy. Unless it was certain, however, that this course was uniformly pursued, it is obvious that there must be some uncertainty in any given case, whether something had not been omitted. There is no doubt that our negligences have been so frequent that our records cannot be relied on, except for what is positively stated. Nor can we say that our inquiries have been sufficiently full originally. We have often failed in learning and still oftener in stating the previous histories of our patients. . . . In the first years we were the most deficient, but we have made our observations with more and more care as we have proceeded.

He wrote these words in his classic report on typhoid fever,[3] communicated to the Massachusetts Medical Society in 1838.

Where did Dr. Jackson get his conviction of the significance of hospital records, which possessed

him when he first took charge of the medical work at the hospital in 1821? Doubtless, the answer is, From his teachers in Great Britain, where he "walked" the hospitals of London and Edinburgh in 1800. It seems evident that the case records of these British hospitals must have been good and

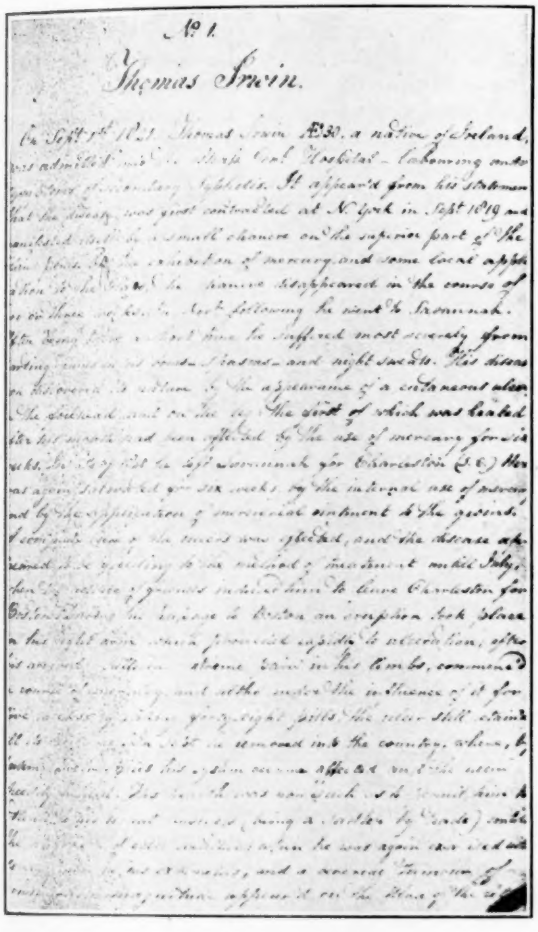


FIGURE 2.

that he took them as a model when the Massachusetts General Hospital was opened. Additional evidence of the importance attached by Scottish hospital physicians to clinical records in the first half of the last century was the custom, introduced by them, of giving the name of the clinical clerk who made the record when they published the notes of the case in a medical paper.

It is of interest to discover and give credit to the physician who first taught and practiced the approved modern plan of making and recording a thorough clinical history and complete physical examination. I am convinced from my reading that this honor belongs to the great French physician, Pierre Charles Alexander Louis. In addition to a careful history of the family, the past diseases and the present illness, we have the testimony of James Jackson[4] that Louis made and recorded more thorough observations than any of his predecessors:

> He noted the actual phenomena present at his examination, depending for this not only on the statement of the patient, but on his own senses, his eyes, his ears, and his hands . . . he was not satisfied with noting the functions, in which the patient complained of disorder, but examined carefully as to all the functions; recording their state as being healthy or otherwise, and even noticing the absence of symptoms which might bear on the diagnosis.

I have heard Osler refer to Louis as the patron saint of the Massachusetts General Hospital, but it was not the influence of Louis that first led James Jackson to keep good records from the opening of the hospital. This is a known fact, since Jackson has left on record the statement that he first learned of Louis's work in 1830. This was nine years after the opening of the hospital. His later debt to Louis, he freely acknowledged. The value of making and recording the physical examination in the manner outlined above, was taught him by Louis. In the first case admitted to the hospital, there was not a single entry on the objective symptoms and signs presented by the patient at the time of his entry, the record dealing solely with the present and past history. This defect was soon remedied, and it was not long before careful notes were made of the objective findings.

In the summer of 1833, James Jackson, Jr., then twenty-three years of age, returned to Boston after nearly two years of study in Paris, carried on chiefly under the direction of Louis. On the morning of October 15, 1833, young Jackson went to the Massachusetts General Hospital, where he examined a patient ill with typhoid fever, who had been admitted on the previous evening to his father's service, and recorded the following notes of the case (I give them in full as they furnish convincing evidence that the quality of this medical record, made one hundred and eight years ago, and the care and thoroughness of the observations were of a high order):

> October 15, 1833 — S. K., aet. 32, unmarried, eyes, hair and complexion dark; maid-servant; born in Salem. Entered the hospital last evening. Ill since seventh instant, perfectly well before; on that day headache, distress and pain in limbs, anorexy, weakness, obliging her to go to bed. Since then she has had bad taste in mouth; no soreness of throat, nor dysphagia; thirst; anorexy; nausea after taking too much liquid, but not at other times; diarrhoea from the first, four or five dejections a day; urine not observed; catamenia on 10th, lasting one day (they had occurred in order the week preceding); no chills; occasional

heat and sometimes sweat at night; no cough; nor dyspnoea, or very little of these; no pain in chest, nor palpitation; headache and dizziness; tinnitus aurium and deafness; no epistaxis; no sleep; some delirium. On the 10th she had the following: Rx. hydr. subm. jalap. āā gr. viii — misce. After this some castor oil; and, the dejections, continuing too frequent, she had fifteen drops of tinct. of opium. After this she had not any important medicine.

The above details were partly from the physician who had attended her.

Now, October 15th, morning; — countenance, as well as mind, very stupid; memory treacherous; cannot tell how long she has been ill, though clear and positive as to existence, or non-existence of certain symptoms; features still, eyes fixed, looking melancholy; face pale or sallow, and evidently emaciated; since her entrance (five p.m. yesterday) no vomiting; great thirst of which only she has complained; two dejections, very watery, not dark, nor painful, quite offensive to smell, one of them a pint; through the night restless and watchful, and probably delirious, though silent, for she arose from bed and went to table for drink in absence of watcher, though she has seemed too feeble to rise up. Lips slightly dry; tongue dry, enlarged, protruded partially, a thin, brown coat over part of lobes; some soreness of gums, which have a white coat and give out a mercurial fetor; abdomen not swollen, nor painful, but a little tender on pressure at epigastrium; some small rose pimples on abdomen, but no sudamina; spleen not felt; skin hot and dry; pulse varies from 112 to 120, small, not soft; resp. 21, not difficult; no dilatation of alae nasi, but slight noise in nose; lies on right side.

How shall the pressing problem of obtaining adequate medical records in small hospitals, as well as large, be solved? Various means have been suggested and applied with success. It is essential that the medical staff be convinced of the necessity of good medical records; this is a matter of education. The reasons for keeping case records have been well stated by Musser[5] as follows:

> Records of cases should be kept for obvious reasons. The habit compels a general survey of the case, and tends to prevent oversight in the examination. It naturally aids in the training of the powers of observation. It teaches a precision in the narration of cases. The memory is aided by repetition and by lack of haste in ascertaining phenomena. The data are on record for more mature reflection, and to aid in the study of the literature of similar cases. The record is of value in case the patient returns for advice after a lapse of time. It may be of medico-legal value. The mental effect on the patient is good, for the taking of notes requires time and accurate, studied observation. In case it is desired to study a large number of cases, records are scientific data.

No patient is adequately cared for by the hospital physician until all information bearing on the case has been elicited and recorded. To do less is to neglect the patient. If the physician realizes this, he can no longer offer the excuse that he is too busy to write notes, for this is tantamount to saying he is too busy to care properly for his patients. Notes do not have to be long to be adequate: a few sentences dictated at the bedside or at the operating table may be worth more than a page written the following day. Every hospital should, if possible, provide a secretary or a dictaphone.

In the preparation of the following suggestions MacEachern's[1] writings have been helpful.

1. Physicians might be convinced of the value of good clinical records if they were required on accepting an appointment to the medical or surgical staff, to sign a statement that they assume responsibility for seeing that all the records of patients under their care are written promptly and completely. This responsibility cannot be delegated to interns or residents.

2. Residents, if properly trained, are of great aid in providing good records, but their work should be supervised by the attending physician, who should always make and record his own observations. Otherwise, it is the record of the resident and not fair to either the physician or his patient.

3. A medical-records committee should be appointed. It is the duty of the chief-of-staff to see that this committee is active and efficient. It should review all records regularly, preferably weekly, and promptly refer back unapproved records to the responsible physician.

4. A medical-records librarian should be provided. She can judge the records quantitatively, if not qualitatively, and can furnish much aid to the medical-records committee.

5. Evaluation of the medical record should first be done by the attending physician. MacEachern says that the practice is increasing of having the attending physician sign a statement reading as follows: "This is to certify that I have carefully reviewed the attached record, . . . and to the best of my knowledge, I find it accurate and complete." He continues:

> To do its work thoroughly and impartially the medical records committee must have the authority of the medical staff to make frank and unprejudiced appraisal of each record. It also has the responsibility of reporting to the medical staff at each meeting regarding deficiencies. Medical records will only attain a proper standard of quality if they are actively reviewed in every hospital in a critical, constructive, and unbiased fashion at stated regular periods, and reports made systematically to the administration and the medical staff.

6. A medical audit may be carried out. This is based on an analysis of the discharge records of all patients and was devised by Dr. Thomas R. Ponton[6]; its introduction was aided by the Association of Record Librarians of North America.

I have observed its successful employment at the Thayer Hospital, Waterville, Maine, where it was introduced by Dr. Frederick T. Hill. It is an additional aid in obtaining good medical records and may prove worthy of adoption by all hospitals.

During the last few years, earnest efforts have been made by laywomen serving as record librarians, as their published papers indicate, to devise means for making hospital physicians record-conscious. Shades of Hippocrates, Louis and James Jackson! What a shock to these pioneers it would be to learn that the physicians of the present generation, who pride themselves on the high position attained by scientific medicine, have neglected the very foundations on which scientific medicine rests—namely, the careful observation and recording of facts obtained by the unaided senses—the eyes, the ears and the hands—of the examiner. Physicians in small hospitals often lament the lack of laboratory facilities for special tests, but they still neglect the all-important methods available to all.

30 Bennet Street

References

1. MacEachern, M. T. *Medical Records in the Hospital.* 374 pp. Chicago: Physician's Record Company, 1937.
2. *Genuine Works of Hippocrates.* Translated by Francis Adams. Vol. 1, 466 pp. London: Sydenham Society, 1889.
3. Jackson, J. *Report on Typhoid Fever.* 95 pp. Boston: Whipple Damrell, 1838. P. 3.
4. Jackson, J. *Memoir of James Jackson, Jr.* 78 pp. Boston: I. R. Butts, 1835.
5. Musser, J. H. *Medical Diagnosis.* Fifth edition. 1105 pp. Philadelphia and New York: Lea Bros. & Co., 1904. P. 21.
6. Hill, F. T. Personal communication.

THE DRUG THERAPY OF MIGRAINE HEADACHE*

Lowell S. Trowbridge, M.A.,† Theodore J. C. von Storch, M.D.,‡
and Major Merrill Moore, M.C., A.U.S.§

BOSTON

UNTIL recently, migraine headache has been most difficult to control. However, since the advent of ergotamine tartrate, this drug has been effective in aborting or terminating 90 per cent of the attacks in 600 cases.[1] In spite of such encouraging results, older and nonspecific drugs continue to be used by those suffering from migraine, probably because of ignorance on the part of the lay public concerning the existence of ergotamine tartrate. To compare the results obtained by specific (ergotamine tartrate) therapy and nonspecific therapy, the effects of various medications used by 200 patients were analyzed in terms of the patients' evaluation of the various drugs. Ergotamine tartrate was employed in the Out-Patient Department of the Boston City Hospital. The other drugs were used by the patients on their own initiative or were prescribed by physicians outside the hospital. All the observations are subjective and were elicited directly from the patients.

The diagnosis of migraine was determined according to criteria previously specified by one of us.[2] The patients were asked to name the drug or drugs used by them to relieve their headaches and to evaluate the relief obtained.

The analysis of patients' reports on their experience with various therapies included only drugs that, in our opinion, had been used by the patient long enough to permit him to evaluate them accurately. There were two steps in the analysis of the data: classification of drugs in groups according to their type or site of action, and a compilation of the number of patients who had used drugs in each group with their subjective opinion of the result of such use. Most patients had employed several—in some cases, as many as ten drugs—in their search for relief.

There were eight groups comprising forty-eight different drugs that had been tried from time to time. Individual patients had used these drugs for various periods, ranging from a single trial to the prolonged use of a drug for more than fifty doses. The therapeutic results, as reported by the patients, are summarized in Table 1.

Table 1. *Comparative Effect on Migraine Headache of Various Drugs.*

Drugs	No. of Patients	Effect: Invariably complete relief	Frequently adequate relief	Usually inadequate relief	Invariably unobtained relief
		%	%	%	%
Vasoconstrictors	54	80	7	4	9
Narcotics	41	44	12	10	34
Barbiturates	25	20	16	12	52
Analgesics	186	16	19	12	53
Gastrointestinal	25	16	8	24	52
Bromides	25	8	20	4	68
Endocrines	15	7	0	7	86
Patent nostrums	29	4	14	10	72

The group of vasoconstrictors included the cerebral vasoconstrictor, caffeine,[3] and the dural vasoconstrictor, ergotamine.[4] Both seemed to be highly effective, although the small number of patients who had tried caffeine (6 cases) precludes an

*From the Neurological Unit, Boston City Hospital, and the Department of Neurology, Harvard Medical School.

†Clinical psychologist, Washingtonian Hospital.

‡Formerly, assistant visiting neurologist, Boston City Hospital, and instructor in neurology, Harvard Medical School.

§Associate in psychiatry, Harvard Medical School, and assistant visiting psychiatrist, Boston City Hospital (on leave of absence).

adequate evaluation of this alkaloid. Eighty per cent of those using ergotamine reported complete relief from the migraine attacks. Because some used the drug orally and others by hypodermic, the percentage relieved is a composite of the relief obtained by the less effective oral and highly effective parenteral routes.[5]

The narcotic group consisted of morphine, pantopon, codeine and scopolamine. Morphine and codeine were most effective, the former being reported to be completely effective in 59 per cent of the patients who used it. However, relief was conditional on the ability of the narcotic to cause sleep or to depress the patient's general physiologic state.

The barbiturates included phenobarbital, Pentobarbital and Allonal. Phenobarbital helped 16 per cent of the patients who tried it.

Under analgesics were classified such drugs as acetanilid, acetylsalicylic acid, amidopyrine, phenacetin and various proprietary remedies containing these substances. Acetylsalicylic acid was successful in giving relief to 10 per cent of the 186 patients assumed to have tested it adequately.

Among the drugs acting on the gastrointestinal system were dilute hydrochloric acid, sodium bicarbonate, Seidlitz powders and various proprietary preparations; Seidlitz powders were the most effective of this group, 18 per cent of its users reporting it helpful. These remedies did not seem to act directly on the headache, but rather relieved the distress due to nausea and vomiting, so that their value in alleviating discomfort from migraine is secondary if not open to question.

Of the bromides, including Bromo-Seltzer and the various bromide salts, Bromo-Seltzer was slightly more helpful than the other drug preparations, but as a whole this group may be said to be relatively ineffective in migraine therapy.

Although not many patients in this study were treated with endocrine substances, the results are included as evidence concerning the casual use of endocrines for migraine. Thyroid, Theelin, Progynon, Hormatone and anterior pituitary extract were administered. Only 1 patient was satisfied with the relief obtained. This patient received pituitary extract. Obviously, these observations are not sufficient to warrant any comment other than that they reflect the results usually obtained from casual application of endocrines in office practice.

Because of the widespread advertising of proprietary medicines described as "headache remedies," it is remarkable how few migraine sufferers have tested them. Of the 29 who did, only 4 per cent obtained adequate relief.

In addition to the cases analyzed above, various drugs acting on the autonomic nervous system were used without success. Seven patients used vasodilators, but none were adequately relieved. Laxatives were reported as fairly helpful by 4 of the 7 patients trying them.

Summary

It may be said that many misinterpretations are made in the evaluation of headache remedies, especially in the therapy of migraine. In this study, there was considerable difficulty with some of the patients in determining whether the particular headache treated by a given drug was actually migrainous, although the patient suffered from migraine attacks at certain times. Side actions of the various drugs may have afforded some secondary relief without affecting the headache itself.

The greatest relief was from drugs in the vasoconstrictor group, consisting mainly of favorable reports on the use of ergotamine tartrate by 80 per cent of its users, in spite of the unpleasant and pronounced side actions. This re-emphasizes the observation that drugs causing vasoconstriction of the branches of the external carotid artery[6] are by far the most successful in terminating or aborting migraine headaches. Analgesics were tested most frequently by the greatest number of cases, but with comparatively unsatisfactory results.

Perhaps newer therapeutic methods, such as oxygen inhalation,[7] vitamin B_1 therapy[8] and arterial ligation[9] will prove effective in the future. Until such time, ergotamine tartrate remains the most effective means of terminating a migraine attack.

References

1. von Storch, T. J. C. Unpublished data.
2. Maddock, C., and von Storch, T. J. C. Unpublished data.
3. Gibbs, F. A., Gibbs, E. L., and Lennox, W. G. The cerebral blood flow in man as influenced by adrenalin, caffein, amyl nitrite and histamine. *Am. Heart J.* 10:916-924, 1935.
4. Pool, J. L., and Nason, G. I. Cerebral circulation; comparative effect of ergotamine tartrate on the arteries in pia, dura, and skin of cats. *Arch. Neurol. & Psychiat.* 33:276-282, 1935.
5. von Storch, T. J. C. On the treatment of migraine. *M. Clin. North America* 25:1317-1330, 1941.
6. Graham, J. R., and Wolff, H. G. Mechanism of migraine headache and the action of ergotamine tartrate. *Arch. Neurol. & Psychiat.* 39:737-763, 1938.
7. Alvarez, W. C., and Mason, A. Y. Results obtained in the treatment of headache with inhalation of pure oxygen. *Proc. Staff Meet., Mayo Clin.* 15:616-618, 1940.
8. Palmer, H. D. Treatment of migraine with vitamin B_1: résumé of one year's experience. *Arch. Neurol. & Psychiat.* 45:368-371, 1941.
9. von Storch, T. J. C. Unpublished data.

INTRINSIC DISEASES OF THE LIVER SIMULATING ACUTE CHOLECYSTITIS

First Lieutenant Knowles B. Lawrence, M.C., A.U.S.,* and Howard M. Clute, M.D.†

BOSTON

IN RECENT years many surgeons have accepted the principle of early operation as the safest method of handling acute cholecystitis. This means that surgery in many such cases will be done as soon as the patient's condition permits and before time has allowed elaborate laboratory studies. It is frequently necessary, therefore, to differentiate clinically between acute cholecystitis and certain other upper-abdominal conditions that may be more suitably handled by conservative means. Our recent experience shows that certain intrinsic diseases of the liver may simulate acute cholecystitis so closely that clinical differentiation is difficult, if not impossible.

The pathologic changes in acute cholecystitis in the early period — that is, the first twenty-four to seventy-two hours after onset — are essentially mechanical in character, as has been demonstrated by a number of investigators at this clinic[1] and elsewhere.[2, 3] The process starts with the blocking of the cystic duct, usually by an impacted gallstone. The resulting edema and venous stasis in the wall of the cystic duct plus obstruction to the outflow of gall-bladder contents set up a vicious circle resulting in a high degree of vascular and lymphatic block of the entire gall bladder. Local ischemic necrosis of the gall-bladder wall may then take place, with perforation resulting if the area involved is large enough.

Changes such as these should, and usually do, produce a fairly standard clinical picture. Initially there is local colicky pain, acute or subacute in onset, as the gall bladder attempts to force an impacted stone through its too narrow cystic duct. Pain of such origin commonly radiates also around the right lower costal margin to the right scapular region. Nausea and reflex vomiting may occur in this stage. As the circulatory changes progress the gall bladder becomes distended, its musculature is less able to contract, so that the colicky pain is superseded by an intense dull ache, a visceral pain due to overstretching of the peritoneal coat. The viscus may then be palpable as a tense and very tender mass below the right liver margin. This is the stage in which the patient is often seen by the surgeon; it may occur a few hours to a few days after onset. Despite the usual absence of bacterial inflammation, there is characteristically a slight rise in temperature and pulse rate and a moderate polymorphonuclear leukocytosis. Later an inflammatory reaction of the serosa may be manifested by tenderness and muscle spasm over the gall-bladder region. Perforation of the gall bladder with peritonitis is usually obvious to the examiner as an acute surgical emergency.

Thus, when one considers acute cholecystitis in the light of the pathologic process, it becomes apparent that certain diseases of its neighbor, the liver, might well simulate its clinical picture. The following morbid mechanisms might be postulated: necrosis in a tumor nodule growing more rapidly than its blood supply, thus causing a considerable reaction on the peritoneal surface; stretching of Glisson's capsule by an underlying hemangioma, abscess or echinococcus cyst of the liver; and a more diffuse hepatic inflammation causing pain through both the above mechanisms plus possible affection of the visceral sensorium — for example, a fulminating acute hepatitis or yellow atrophy. Fever, leukocytosis, systemic debility or reflex gastrointestinal symptoms may be as commonly associated with certain of these conditions as with acute cholecystitis.

At the Massachusetts Memorial Hospitals we have encountered several cases of intrinsic liver disease which simulated acute cholecystitis so closely that the diagnosis was often difficult and uncertain. These cases, with comments on their diagnosis and management, are as follows:

Case 1. A 56-year-old white woman entered the hospital complaining of right-upper-quadrant pain of 5 days' duration. Fifteen years and 2 years previously she had had attacks of pain and indigestion and x-ray films were said to have shown trouble with the gall bladder. Similar symptoms set in 6 weeks before admission. She had had some vomiting also and diarrhea without blood. Five days before admission severe right-upper-quadrant pain began with radiation to the right posterior shoulder region, mild chills and fever. There was a 34-pound weight loss in 3 months.

On examination the patient appeared in acute pain. A tense, rounded, very tender mass, the size of a small fist, was felt in the gall-bladder region. The liver edge could be palpated 5 cm. below the right costal margin, rounded and slightly tender. On rectal examination a hard, polypoid mass involving the anterior rectal wall and invading the pararectal tissues, an obviously malignant neoplasm, was found. The admission temperature was 102.4°F., the pulse 100, and the white-cell count 15,000, with 84 per cent polymorphonuclears.

Laparotomy was performed shortly after admission, and the mass felt preoperatively was found to be a hard tumor

*Assistant in surgery, Boston University School of Medicine, and assistant surgeon, Massachusetts Memorial Hospitals (on leave of absence).

†Professor of surgery, Boston University School of Medicine; surgeon-in-chief, Massachusetts Memorial Hospitals.

nodule imbedded in the liver. Just medial to it lay the virtually normal gall bladder. There were multiple tumor nodules throughout the liver, and a biopsy of one of these showed an anaplastic, rapidly growing metastatic adenocarcinoma. The patient died 6 weeks later.

The clinical picture in this case so closely simulated that of acute cholecystitis that early operation seemed the wiser course, despite the knowledge preoperatively of the patient's carcinoma of the rectum. Had the routine rectal examination been omitted, as it is at times, unfortunately, the case for acute cholecystitis would have been even stronger. We surmise that the symptoms and signs in this case were due to necrosis within the large tumor nodule lying just to the right of the gall bladder.

CASE 2. A 67-year-old white man, a physician, was admitted because of bowel symptoms and weight loss. Five years previously a resection of 12 cm. of transverse colon had been performed for a "malignant polyp" at another hospital.

The physical examination was essentially negative. The patient was studied in great detail without definite findings. Three weeks after admission he developed rather suddenly a severe right-upper-quadrant pain with tenderness and spasm in the right subcostal region. The liver edge was palpable and possibly somewhat irregular. The temperature was 99.6°F. and the white-cell count 11,300, with 87 per cent polymorphonuclears.

A previous cholecystogram had demonstrated a probable chronic cholecystitis and cholesterosis. No stones were seen. In view of the clinical picture at this time a diagnosis of acute cholecystitis was considered, but the probability that the symptoms were due to metastatic liver disease was so strong that operation seemed unwarranted. The symptoms subsided somewhat, and the patient died several weeks later of general carcinomatosis, including the liver, and terminal pneumonia.

CASE 3. F. B., an 83-year-old white man, was admitted to the Massachusetts Memorial Hospitals on April 16, 1942, complaining of severe right-sided abdominal pain for 4½ days' duration. At first this pain was felt in the right midabdomen, then 24 hours later worked up into the right upper quadrant and beneath the costal margin, where it persisted as a fairly constant, severe aching pain. The pain did not radiate, but was severer when the patient breathed deeply or moved about.

During the previous year the patient had become increasingly constipated and had experienced frequent bouts of painless vomiting lasting a day or more, usually occurring when he was constipated. There was no pain associated with this. He had been passing gas satisfactorily up to the time of admission. There was no history of chest pain. The patient's health prior to this trouble had been reasonably good for his age. He had had a suprapubic prostatectomy for benign prostatic hypertrophy 3 years previously.

Examination showed an emaciated elderly man in obvious pain lying on his left side with the legs drawn up. The rectal temperature was 101°F., the pulse 92, and the blood pressure 118/80. Marked generalized arteriosclerosis was noted. The heart and lungs were normal for the patient's age. The abdomen was slightly distended and was resonant throughout. It was generally soft except for definite spasm of the right-upper-quadrant muscles near the costal margin and definite tenderness over this same area. A poorly defined mass, possibly 6 cm. in diameter, could be felt and percussed in this area and seemed to come from beneath the costal margin. Peristalsis was somewhat hyperactive throughout the abdomen.

The white-cell count was 10,200, with 78 per cent polymorphonuclears, and the red-cell count 3,190,000, with a hemoglobin of 64 per cent. The nonprotein nitrogen was 43 mg. per 100 cc., and the icteric index 10. Urinalysis revealed a trace of albumin, many white cells and rare red cells. The urinary diastase was less than 4 units. A flat x-ray film of the abdomen showed no opaque calculi. The colon appeared distended with gas. A barium enema done the following day showed a diverticulosis and a diverticulitis of the sigmoid and colon without obstruction.

A provisional diagnosis of acute cholecystitis was made. It was thought that the process was localized and would probably subside with conservative treatment. In view of this and the patient's extreme age, operation was deferred.

The patient was given sulfadiazine by vein and by mouth and a sufficient quantity of intravenous fluids. He continued to run a low-grade septic course with the temperature ranging between 99.6 and 102°F. (rectal). The white-cell count varied between 11,000 and 17,000. The pain and tenderness persisted. The right-upper-quadrant mass became larger and considerable fluid accumulated in the abdomen. The patient was thought to have developed a pericholecystic abscess.

Operation was therefore performed, with intent to drain the gall bladder, 8 days after admission. The finding, however, was an enlargement of the liver by irregular infiltrations with yellow tumor tissue. The biopsy diagnosis was primary hepatoma. The gall bladder was not inflamed. The patient went downhill rapidly and died 36 hours later.

Autopsy revealed massive enlargement of the liver by primary hepatoma, which in two places had grown into the stomach wall. The gall bladder showed no disease.

This case closely resembled one due to acute cholecystitis. Even in retrospect, no direct clinical leads to the correct diagnosis are apparent.

CASE 4. A 36-year-old Negro entered the hospital complaining of severe retching, vomiting and malaise of 3½ days' duration. He denied real pain — only a slight upper-abdominal soreness. The vomitus was reflex rather than obstructive in type, and the patient's evacuations continued fairly normally. He dated his illness from the inhalation of fumes from an accidentally broken fire-extinguisher bulb containing carbon tetrachloride. Eighteen months before entry, on a previous admission for gonorrheal epididymitis, the liver edge had been felt three fingerbreadths below the costal margin; the patient was given 40 gr. of sulfanilamide daily for 6 days for his gonorrheal infection. He was known to have been a chronic alcoholic for several years. There was no history of definite gastrointestinal symptoms prior to the present illness.

On examination the temperature was 102°F., and the pulse 100. The patient was acutely ill, groaning with pain and rolling from side to side with the thighs flexed on the abdomen. The upper two thirds of the abdomen, particularly on the right side, was nearly boardlike and exquisitely tender. This splinting, plus a well-developed musculature, prevented satisfactory palpation or even percussion of the upper abdomen. The liver margin could

not be palpated. Jaundice was not apparent, as the patient was a Negro and was seen after nightfall. The white-cell count was 31,000. The urine contained a trace of bile. X-ray films of the abdomen and diaphragmatic area showed the liver somewhat enlarged, but no free gas or other abnormalities. Despite an atypical history, it was believed that the signs were those of an acute upper-abdominal peritonitis, possibly from a perforated gall bladder or peptic ulcer, and that immediate operation was imperative.

On opening the abdomen an acute hepatitis with free bile-stained peritoneal fluid and toxic regional lymphadenitis was found. A biopsy specimen from the liver was diagnosed acute hepatic necrosis (central type). Following the operation the patient declined rapidly and died 4½ days later. An autopsy revealed a hemorrhagic central necrosis of the liver, probably due to carbon tetrachloride poisoning, toxic nephrosis and pulmonary edema.

This case illustrates the well-known fact that certain cases of acute hepatitis present a clinical picture difficult to differentiate from acute surgical conditions of the upper abdomen. Knowledge of this combined with the history of exposure to a hepatotoxic drug should make the surgeon doubly wary.

In studying the literature, we were able to find little on the subject of diseases of the liver simulating acute cholecystitis. However, the following conditions, which at times have produced similar clinical pictures, are mentioned; ruptured hemangioma, spontaneous rupture of the liver and spontaneous subglissonian hemorrhage, simple cysts of the liver with or without rupture, tuberculoma and gumma, echinococcal cyst, amebic abscess, pyogenic abscess and neoplasms of the liver, primary or metastatic.

Conclusions

Acute hepatic disease may simulate acute cholecystitis as to sudden onset, low fever, an elevated white-cell count and a tender mass in the right upper quadrant.

A history of exposure to a hepatotoxic drug should lead one to consider the possibility of acute yellow atrophy.

The clinical picture of acute cholecystitis may also be simulated by primary or metastatic cancer of the liver, particularly when secondary hemorrhage or necrosis has occurred. A history of previous malignancy should make one suspicious of this.

These and other intrinsic diseases of the liver are occasionally difficult to differentiate from acute cholecystitis.

References

1. Clute, H. M., and Lembright, J. F. Immediate surgery in acute cholecystitis. *New Eng. J. Med.* **218**:72-75, 1938.
2. Womack, N. A., and Bricker, E. M. Pathogenesis of cholecystitis. *Arch. Surg.* **44**:658-676, 1942.
3. Glenn, F., and Moore, S. W. Gangrene and perforation of the wall of the gallbladder; a sequela of acute cholecystitis. *Arch. Surg.* **44**:677-686, 1942.

PRIMARY CARCINOMA OF THE APPENDIX ASSOCIATED WITH ACUTE APPENDICITIS

Report of a Case

Edward L. Young, M.D.,* and First Lieutenant Stanley Wyman, M.C., A.U.S.†

BOSTON

PRIMARY carcinoma of the appendix must be differentiated from carcinoid of the appendix and carcinoma of the cecum. Failure to distinguish between these conditions has led to an unfortunate confusion in the literature.

Carcinoid is a disease usually found unexpectedly by the pathologist. Eighty-two per cent of cases occur in females,[1] and the greatest incidence is found in the third decade.[2] Such cases comprise less than 0.4 per cent of all intestinal cancers.[3] Carcinoids are usually firm ovoid tumors, often yellow, located near the tip of the appendix. They are composed of cells originating from the Kultschitzky cells in the bases of Lieberkuhn's glands. Because the cells contain silver-reducing granules, the tumors are often called "argentaffinomas." They resemble basal-cell epitheliomas in that they often form sheets or islands of cells with occasional mitoses. In general, they act as benign tumor, but metastases to the liver and regional lymph nodes have been reported.

Carcinoma of the cecum most frequently takes the form of a large fungating mass that may occlude the lumen of the appendix or infiltrate its base, at times giving rise to symptoms of appendiceal obstruction. Many cases of carcinoma of the cecum are reported in the literature, in contrast to primary carcinoma of the appendix.

True carcinoma of the appendix is primary in that organ and is usually colloid in type.[4] It causes no specific signs or symptoms, but at times the patient may give an atypical history of appendicitis or may have recurrent attacks of right-lower-

*Surgeon-in-chief, Faulkner Hospital; visiting surgeon, Massachusetts General Hospital.

†Formerly, house officer, Faulkner Hospital.

quadrant pain. It may make itself known as a mass in the abdomen, cause a generalized peritonitis by perforating the bowel or obstruct the lumen of the appendix. The literature of the last ten years contains many reports of carcinoma of the appendix, but close examination reveals only 4 cases of apparently true primary carcinoma — Darnall and Kilduffe,[5] Blumenkopf,[6] Heine[7] and Frauenthal and Grausman.[8]

Case Report

A 36-year-old married man entered the Faulkner Hospital on June 24, 1940, complaining of pain in the abdomen. Two weeks before entry, he had an episode of pain in the abdomen preceded by soreness low in the back. Abdominal pain lasted 4 or 5 days and was accompanied by fever, but there was no nausea or vomiting. A physician told the patient that he had mild appendicitis and that if he had a recurrence he should be operated on. On the day before entry, the patient noticed slight twinges of pain in the right lower abdomen, but he went to bed and slept well. He awoke with a sensation of soreness in the lower abdomen. During the course of 2 hours, the pain increased rapidly in severity, and by 11 a.m. the patient was almost doubled up with crampy abdominal pain. There was no nausea or vomiting, and the bowels moved normally on the day of entry. There was no pain or burning on urination, and no hematuria, pyuria, recent cold or pain in the chest. The past and family histories were irrelevant.

Physical examination revealed a well-developed and well-nourished man lying in bed with the legs bent. The height was 5 feet, 8 inches, and the weight 200 pounds. The temperature was 101°F., the pulse 74, and the respirations 20. The tongue was coated, and the throat slightly injected. The heart and lungs were normal. There was no costovertebral tenderness. The abdomen was flat, and no organs or masses were palpable; there were no hernias. Slight spasm was apparent in the right lower quadrant, with very definite acute tenderness in a sharply localized area over McBurney's point. Pain and rebound tenderness followed pressing in the left lower quadrant. Rectal examination was negative. The reflexes were physiologic.

Laboratory studies showed a white-cell count of 10,500 with 79 per cent polymorphonuclear leukocytes. Examination of the urine was negative. A flat plate of the abdomen was negative for localizing signs and for kidney stones.

A diagnosis of acute appendicitis was made. Under spinal anesthesia, a right pararectus incision was made. When the abdomen was opened, some cloudy fluid was present, and the appendix was found to be greatly swollen and stiff, with one gangrenous area. The base was edematous and porky in consistence. The appendix was excised at its base, the stump buried, and the abdomen closed in layers without drainage. At this time, there was no suspicion that cancer was present.

Pathological examination showed an appendix measuring 6 cm. in length and 1.5 cm. in diameter. The surface varied from red to pink and showed occasional patches of yellowish fibrin. The wall was moderately distended, and at a point 2 cm. from the tip, there was a constricted area. The lumen was found with difficulty, especially in the proximal portion. The wall was markedly thickened, the cut surface being glistening and white. The distal half of the appendix showed a fairly definite lumen filled with grayish fluid and a few smooth, hard, black masses measuring up to 0.3 cm. in diameter. When the larger masses were cracked, they were found to contain seeds.

Microscopically, three sections showed infiltration of the wall by small islands of cells, which frequently occurred as signet cells and were surrounded in part by bluish-staining mucoid material. In two sections, a rather broad area in the mucosa, although not extending entirely through the surface, presented an increase in connective tissue through which were scattered individual signet cells and small cords of cells. An occasional luminated structure was found, and frequent mitoses were present. In addition, the mucosa showed patches of necrosis, and the lumen contained polymorphonuclear leukocytes in several sections. On the outer surface, there was a mass of fibrinopurulent exudate, and, in one region, large numbers of bacteria, occurring as an abscess in the periappendiceal fat tissue. Figure 1 shows the histologic picture of the tumor. Diagnosis: primary carcinoma of the appendix, occurring chiefly as the colloid type, and acute appendicitis, with abscess formation and masses of bacteria on the serosal surface.

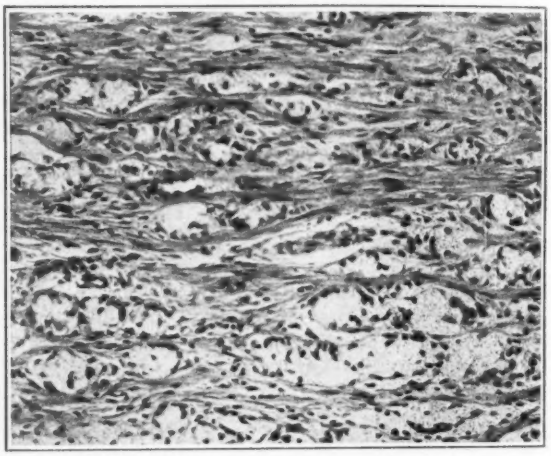


Figure 1. *High-Power View of a Section of the Tumor.*

Three weeks later, an ileotransverse colostomy was performed. The germinal ileum for a distance of 60 cm. was found adherent to the cecum. In addition, there was a Meckel's diverticulum 45 cm. from the cecum. The patient made an uneventful recovery from this operation, and 10 days later, a right colectomy was done, the terminal 45 cm. of ileum, the cecum, ascending colon and hepatic flexure being removed. Histologic examination showed a few small islands of colloid carcinoma in the outer portion of the muscularis at the site of the appendiceal stump, but none elsewhere; the regional lymph nodes showed chronic inflammation but no evidence of tumor.

At a follow-up examination more than two years following the last operation, the patient stated that he had been symptom free and had been doing hard physical labor; neither x-ray nor physical examination revealed evidence of recurrence.

Summary and Conclusions

The literature for the past ten years is reviewed, true carcinoma confined to the appendix being found to be quite rare.

A case of acute appendicitis complicated by colloid carcinoma is reported.

Colloid carcinoma of the appendix may cause no specific symptoms or signs, and since carcinoma may be indistinguishable grossly from acute inflammation, microscopic examination of all appendices removed at operation should be done.

References

1. Vance, C. A. Primary carcinoma of vermiform appendix. *Am. J. Surg.* 24:854-862, 1934.
2. Leonardo, R. A. Primary carcinoma of the appendix vs. carcinoid. *Am. J. Surg.* 22:290-294, 1933.
3. Norment, W. Tumors of the appendix. *Surg., Gynec. & Obst.* 55:590-596, 1932.
4. Elting, A. W. Primary carcinoma of the vermiform appendix with report of three cases. *Ann. Surg.* 37:548-574, 1903.
5. Darnall, W. E., and Kilduffe, R. A. Carcinoma of the appendix in a girl of twenty. *Am. J. Surg.* 17:63-65, 1932.
6. Blumenkopf, D. Beitrag zur Kenntnis der primären, echten Carcinome der Appendix. *Ztschr. f. Krebsforsch.* 43:182-194, 1935.
7. Heine, J. Appendicitis und Karzinom der Appendix. *Zentralbl. f. Chir.* 62:2601-2603, 1935.
8. Frauenthal, M., and Grausman, R. I. Primary carcinoma in the vermiform appendix. *Am. J. Surg.* 19:118, 1933.

MEDICAL PROGRESS

THE BILE PIGMENTS (concluded)*

CECIL JAMES WATSON, M.D.†

MINNEAPOLIS

Recent clinical advances. In 1936, a further modification of Terwen's method for the quantitative determination of urobilinogen in urine and feces was described.[71] It was shown that the color intensities of mesobilirubinogen-aldehyde and stercobilinogen-aldehyde, as developed with Ehrlich's reagent in this method, were identical. More recently, this has been confirmed by means of the Evelyn photoelectric colorimeter, and the method has been applied to it,‡ with excellent results.

Studies of jaundice, with particular reference to the daily excretion of urobilinogen in the feces and urine,[72, 73] have shown that helpful fundamental and diagnostic information may often be gained. With a modification of Rich's[74] classification of jaundice, as given below, the various forms noted are characterized in the main by urobilinogen excretion as indicated. The normal range was found to be 40 to 280 mg. per day for the F.U. (feces urobilinogen) — usually 100 to 200 mg. — and 0 to 3.5 mg, per day for the U.U. (urine urobilinogen) — most frequently 0.5 to 1.5 mg. The value for the feces is an average for a four-day period, whereas that for the urine is for 24 hours.[71–73, 75]

I. *Retention jaundice* may be defined as hepatocellular inability to remove bilirubin from the circulating blood, with resultant accumulation. There is an indirect or delayed van den Bergh reaction and no bilirubinuria.

A. *Hemolytic jaundice* may be spheroidocytic or macrocytic, and the former may be familial or acquired in type. The F.U. ranges from 300 to 4000 mg. per day, usually 600 to 2000 mg., and the U.U. varies from 1.0 to 200 mg. per day, usually 5.0 to 30.0 mg.

The feces urobilinogen is commonly higher in patients with marked anemia or with hemolytic crises, but there is not a strict correlation.[76] Cases are seen with high values but relatively little anemia.[76] Contrary to frequently expressed belief, cases are often encountered with a marked increase in feces urobilinogen, but with a normal amount in the urine.[76] Such patients may have marked anemia, but relatively little, or even no, jaundice.[1, 76] In general, it may be stated that the more anemia, the less jaundice and urobilinogenuria and vice versa. The immediate period of hemolytic crises constitutes an exception to this, however.

B. *Constitutional hepatic dysfunction* consists in constitutional hepatocellular inferiority in bilirubin excretion into the bile. This condition may or may not be familial. It has been described under various names and by different investigators,[1, 77–79] more recently by Dameshek[80] under the designation of "familial nonhemolytic jaundice." The abnormality is characterized by simple accumulation of bilirubin; there is neither splenomegaly, spheroidocytosis or reticulocytosis nor any evidence of hepatic functional impairment other than faulty excretion of bilirubin.

The F.U. ranges from 100 to 200 mg., and the U.U. from 0.5 to 3.5 mg. per day.

C. Various factors, such as chronic passive congestion (often with pulmonary infarcts),

Reprints of articles in this series are not available for distribution, but the articles will be published in book form. The current volume is *Medical Progress: Annual, Vol. III, 1942* (Springfield, Illinois: Charles C Thomas Company, 1942. $5.00).

*From the Division of Internal Medicine, University of Minnesota Hospital.

†Professor of medicine, University of Minnesota; chief of Medical Service, University of Minnesota Hospital.

‡Watson, C. J. Unpublished data.

pneumonia, virus and other infections, and poisons like arsphenamine and sulfanilamide, may produce a *mild retention jaundice*. This may become more marked, with developing evidence of regurgitation jaundice, or it may recede without this. Pure retention jaundice may be noted in the convalescent or later stages of any type of hepatitis. Not infrequently, especially with jaundice due to heart failure or pneumonia, a mild hemolytic component is present, as reflected in an elevated feces urobilinogen. The urine urobilinogen is nearly always elevated.

The F.U. varies from 100 to 500 mg. per day, usually 200 to 300 mg., and the U.U. from 5 to 100 mg. per day, usually 10 to 30 mg.

II. *Regurgitation jaundice* is caused by leakage or regurgitation of bile into the blood. Depending on the factors given below, this is due either to increased intrabiliary pressure with actual "rhexis" of the bile capillaries (especially ampullas) or smaller ducts,[81] or to damage of these structures, resulting in increased permeability.[82, 83] In either event, the bile probably gains access first to the lymph spaces of Desse, thence to the thoracic duct and the blood.[81, 82, 84] The van den Bergh reaction is prompt or biphasic and bilirubinuria is present.

A. The *mechanical type* is caused by regurgitation of bile due to increased intrabiliary pressure.

1. *Cancer of the biliary tract* includes carcinoma, either primary or metastatic, and tumors of the lymphoblastoma group. The term "biliary tract" refers to the main hepatic ducts, the common hepatic duct, the common bile duct or the ampulla of Vater. Cancer involving these structures may be primary or secondary. A smooth, nontender, distended gall bladder is often palpable. There is complete biliary obstruction in about 90 per cent of cases.

The F.U. is less than 5 mg., and the U.U. less than 0.5 mg. per day.

Incomplete biliary obstruction is encountered in less than 10 per cent of cases.[85] This group includes polypoid and necrotic tumors and minute ampullary or common-duct carcinomas.[73, 75] It may be emphasized that the depth of jaundice is not determined solely by the degree of biliary obstruction. Decreased bilirubin formation, or "throttling" of blood destruction following blood loss, results in a decrease of jaundice even though the biliary obstruction may remain complete.[85, 86]

2. With *calculi*, the jaundice is usually fluctuant or intermittent. Colic and chills are commonly noted. Incomplete biliary obstruction is present in approximately 90 per cent of cases.[85]

The F.U. ranges from 7.0 to 600 mg., and the U.U. from 0 to 50 mg. per day. This variation depends on several factors. With rapidly diminishing jaundice after spontaneous release of the obstruction, large amounts may be encountered for a short period. With low-grade obstruction, the amount may be within the normal range, although in some cases of this type it may be markedly decreased, probably because of a diminished rate of blood destruction. An impacted stone might be expected in a case with complete biliary obstruction. In my experience, this has usually not been found. Several cases have been observed in which the stone or stones were entirely loose in the duct and in which the reason for the complete obstruction was not apparent[85]; conversely, impacted stones have been noted in several cases with incomplete obstruction.[73]

The amount of urobilinogen in the urine depends on several factors, among which may be mentioned: the duration of the biliary obstruction and whether biliary or obstructive cirrhosis has developed; the presence or absence of cholangitis; and the degree of obstruction. Small amounts of urinary urobilinogen indicate hepatic functional impairment if but small amounts are present in the feces. This is probably true in jaundice of whatever cause.[73]

3. In the majority of cases of *postoperative or benign stricture*, the obstruction is incomplete, but it appears that complete obstruction is encountered more frequently than with a common-duct stone.[85]

The F.U. ranges from 0 to 300 mg., and the U.U. from 0 to 50 mg. per day. This variation of urobilinogen depends on the factors discussed in the foregoing paragraph.

4. *Chronic pancreatitis* causes jaundice but rarely; data on urobilinogen excretion are available from only 2 cases.[85] In one of these, the icterus was mild, and the biliary obstruction was not high grade; in the other, the clinical picture was that of carcinoma of the head of the pancreas, with the exception that the feces contained 9 to 22 mg. of urobilinogen per day during two four-day collections. The amount in the urine was negligible. This patient presented an easily palpable, nontender, distended gall bladder. At operation, the surgeon thought he was dealing with a carcinoma of the pancreas and performed a cholecystgastrostomy. The patient died of a postoperative hemorrhage (vitamin K at that time had not become available). Histologic

study of the pancreas obtained at autopsy first clarified the diagnosis, revealing a diffuse chronic fibrous pancreatitis.

B. The *parenchymal type* is any regurgitation jaundice due to diffuse liver damage (not secondary to mechanical obstruction). Acute and chronic hepatitis, damage due to toxins and chemicals, cirrhosis, diffuse carcinomatosis, and chronic passive congestion are included. Regurgitation of the bile is mainly the result of increased permeability of the bile capillaries (ampullas and small bile ducts and, at least in some cases, of intrahepatic bile-duct or bile-capillary obstruction, because of swelling of the liver cords, edema of the spaces of Desse[36] or fibrosis in the portal areas of the liver lobules.

The F.U. varies from 0 to 1000 mg. per day, usually 10-300 mg., and the U.U. from 0 to 300 mg., usually 0.5 to 100 mg. Of 57 cases of various types of parenchymal jaundice, only 2 (3.5 per cent) exhibited less than 5 mg. of fecal urobilinogen per day. Six were found to have less than 1 mg., and 4 less than 0.3 mg. in the twenty-four-hour urines.[85] These values may be compared with those given above for biliary-tract cancer and the calculous group.

1. *Hepatitis* may be divided into the groups shown in Table 1, with their corresponding

TABLE 1. *Types of Hepatitis with Particular Reference to Urobilinogen Excretion.*

TYPE	UROBILINOGEN EXCRETION F.U. mg./day	U.U. mg./day
Acute		
Early period (2 to 4 days)	10–100	10–100
Peak of jaundice (4 to 8 days)	0–20	0–10
Diminishing jaundice (7 to 30 days)	50–600	10–300
Subacute (1 to 2 months)	10–1200	0.5–300
Subchronic (2 to 6 months)	10–1200	0.5–300
Chronic (cirrhosis)		
With marked jaundice	10–1200	0.5–300
With mild or no jaundice	50–300	0.5–30

ranges of urobilinogen excretion. It is seen that, in some cases of acute hepatitis, urobilinogen is absent from the urine and feces during the peak of the jaundice. Insufficient data are available regarding the actual percentage of cases with complete exclusion of bile from the intestines during the height of the disease. The majority of cases that have been studied were first seen when the jaundice had already been present for some time and was beginning to diminish. From the available evidence, there is little doubt that a temporary, complete exclusion is not uncommon. Judged by simple inspection or by qualitative tests alone, however, complete exclusion has undoubtedly been believed to be commoner than it is. Grossly acholic feces may contain from 10 to 15 mg. of urobilinogen per day; correspondingly, a twenty-four-hour-urine sample may exhibit a negative qualitative Ehrlich reaction, and yet by the quantitative method[73, 75] as much as 15 mg. per day may be detected. During the third or receding stage of acute hepatitis, urobilinogen usually reappears in the urine in large amounts. Serial qualitative tests are of much value at this point, since they often reveal the first evidence of beginning improvement — that is, the re-establishment of bile flow to the intestine. From this point on, the progress of convalescence may be followed by observation of the urobilinogen reaction each day. In a small percentage of cases of acute catarrhal jaundice, urobilinogenuria fails to appear during the convalescent period. It remains to be determined whether these are examples of catarrhal jaundice in the true sense of the word — a "catarrhal choledochitis"[87] — or whether an actual hepatitis.

As noted above, a considerably increased fecal urobilinogen excretion may be observed as the jaundice diminishes in acute hepatitis and also, for longer periods and in greater degree, in the more prolonged cases, including some of those that progress to cirrhosis. There is every reason to believe that these increases are often associated with an increased rate of blood destruction. Outspoken hemolytic anemia may develop, with macrocytosis and increased reticulocytes.[73, 76, 78] Splenic enlargement is usually marked. In van den Bergh and Kamerling's[88] fatal case of this type, there was a large amount of hematin in the circulating plasma. In passing, it might be noted that hematinemia has been emphasized repeatedly as an evidence of liver damage. Whether this is actually hematin or Fairley's[89] methemalbumin has not been determined.

2. *Toxins*, such as those occurring in pneumonia, peritonitis, hemolytic-streptococcus septicemia, gas-bacillus sepsis and other severe toxemias, may produce liver damage. F.U. ranges from 100 to 400 mg., and the U.U. from 10 to 200 mg. per day.

3. *Poisons*, such as arsphenamine, cinchophen, phosphorus, trinitrotoluene, sulfanilamide and many other substances, may result in liver damage. The F.U. varies from 10 to 1000 mg., and the U.U. from 0.5 to 300 mg. per day.

The jaundice seen following arsphenamine or cinchophen may be associated with almost complete suppression of bile flow — in some cases, quite complete. Arsphenamine jaundice may

simulate acute or subacute hepatitis, or so-called "catarrhal jaundice" quite closely. On the basis of clinical and histologic studies (liver biopsy) in 10 cases, Roholm and Krarup[90] have recently stated that arsphenamine simply lowers the resistance of the liver to the virus of epidemic hepatitis. Hanger and Gutman[91] have described cases of arsphenamine jaundice similar to what Eppinger calls the "cholangiolitic type" of catarrhal jaundice in distinction to the ordinary, hepatocellular variety. Although there is no doubt of the existence of the two clinical types, there are many borderline cases, and so far as can be determined at present, there are no disturbances of pigment metabolism that are distinctive.

Cinchophen jaundice may likewise simulate acute hepatitis, especially in the appearance of the pigments. In a case previously recorded,[73] there was a history of recent ingestion of pills (probably cinchophen) for "rheumatism." Painless, deep jaundice, with anorexia and nausea, developed. At the height of the jaundice, the F.U. was 10.2 mg., and the U.U. 3.8 mg. When the jaundice had diminished, the former was 280 mg., and the latter 207 mg. This case illustrates well the high-grade but incomplete biliary obstruction, the importance of evaluating a relative increase of urobilinogen in the urine in favor of liver damage and, finally, the large amount in the urine during the re-establishment of bile flow, owing to residual disturbance of liver function.

Jaundice following sulfanilamide is rarely intense or associated with a very marked suppression of bile flow. There may be a prominent hemolytic factor, with outspoken anemia and increased fecal urobilinogen.[92] Occasionally, cases are seen in which the jaundice deepens rapidly and death is due at least in part to severe hepatic injury, even acute atrophy. In my experience, however, jaundice of this degree has been observed only when there was reason to believe that the liver was damaged before the administration of sulfanilamide — for example, in the presence of severe infections or toxemias or when the drug was given to a patient also receiving arsphenamine treatment for syphilis.

4. Cirrhosis of the liver is of various types. In the foregoing discussion of "hepatitis," the chronic form was noted as being synonymous with cirrhosis. This does not indicate that all types of cirrhosis follow hepatitis. On the contrary, many are probably related to other factors, of which fatty liver, deficiency states (including chronic alcoholism) and various poisons, notably cinchophen and arsphenamine, may be emphasized. From the standpoint of the bile pigments, however, no features differentiate the various etiologic factors. This is also true of hemochromatosis, although it may be noted that jaundice is usually not prominent in this disease.

5. In some cases of *diffuse carcinomatosis*, hepatic metastases are sufficiently extensive to impair liver function markedly. Considerable jaundice may be noted, even though the main hepatic ducts are uninvolved. Marked urobilinogenuria may occur,[85] and the clinical picture may closely simulate cirrhosis of the liver.

6. *Chronic passive congestion* has already been referred to as a cause of retention jaundice. In severe cases of so-called "cardiac jaundice," regurgitation jaundice is nearly always present as well.[93] Pulmonary infarcts are commonly found.[36] Urobilinogenuria is usually noted, and is often marked. Edelman and his co-workers[94] found an excess of urobilin in 88 per cent of their cases of heart failure. The presence of renal insufficiency or azotemia usually prevents or reduces urobilinogenuria.[95] Correspondingly, when crystalline stercobilin is administered intravenously in a patient with both hepatic and renal impairment, its elimination in the urine is markedly retarded.[1]

Pulmonary or myocardial infarction is often productive of marked urobilinogenuria. Head* has shown that serial qualitative urine urobilinogen tests are helpful in the diagnosis and care of coronary thrombosis and its complications. There is considerable reason to believe that this indicates liver damage due to substances coming from the infarct. Urobilinogenuria occurring after a ruptured tubal pregnancy has been similarly explained.[96] After an attack of coronary thrombosis productive of an infarct, the urobilinogen reaction rarely becomes positive before the end of the first twenty-four hours and usually not before two or three days, quite in contrast with an acute biliary colic or acute cholecystitis, in which the reaction often appears almost at once. In the latter condition the urobilinogenuria is believed to be due to lymphatic drainage of bacteria or toxic material from the gall bladder into the liver, with resultant hepatitis or liver-function impairment.[73]

The simple qualitative test for urobilinogen[71] often yields valuable information, although it is true that in many cases nothing very decisive can be found without quantitative determination of the per-diem amounts in the feces and urine. Positive reactions in the feces usually indicate patency of the biliary tract, or at least that biliary obstruction

*Head, D. P. Unpublished data.

is not complete. Very weakly positive reactions are difficult to evaluate since they may be noted in the presence of complete biliary obstruction, such as that due to cancer. These reactions are probably explained by traces of urobilinogen derived from bile-stained epithelial cells or, in some cases, from bilirubin contained in the serum of blood that has entered the intestines from some source of hemorrhage in a patient with deep jaundice. One such case was seen recently in which it appeared probable that 11 mg. per day of fecal urobilinogen was on this basis. The amount of bilirubin provided by bile-stained mucosa probably never exceeds 5 mg. per day (in terms of urobilinogen), and yet this or smaller amounts may be sufficient to give weak Ehrlich reactions, which are likely to be confusing in diagnosis. If the qualitative test alone is to be used, one should rely only on a series of entirely negative or outspokenly positive reactions in attempting to assay the degree of biliary obstruction. Serial tests are also highly desirable for the urine.

In cases of liver damage, especially cirrhosis, the fluctuation in urobilinogen excretion from day to day, and even at different hours of the day, is often striking. Persistently negative reactions in patients with deep jaundice usually signify complete obstruction, although there are definite exceptions to this. Strongly positive reactions in patients with marked jaundice, but without any suggestion of cholangitis or biliary cirrhosis that might be secondary to a common-duct stone, are nearly always indicative of a parenchymal jaundice, due either to hepatitis or to cirrhosis. In a study of 80 cases of painless jaundice, White[97] found positive urinary urobilinogen reactions in 88 to 100 per cent, depending on the stage of the disease. This study was carried out with the Wallace and Diamond[98] method, which is simply a series of dilutions of the qualitative test. In a later paper, White and his associates[99] compared this method with those of Sparkman[100] and Watson.[71] The former had been proposed as a simpler quantitative method. It employed single samples of urine or feces rather than daily collections. Various disadvantages and errors in this technic were subsequently noted by Watson and Bilden.[75] In the comparative study of White et al.,[99] the Sparkman method was found to have no advantage over that of Wallace and Diamond. Neither method was as accurate as the Watson[71] modification of Terwen's[101] procedure.

The qualitative test for urobilinogen may be masked by the presence of large amounts of bilirubin, especially when converted to biliverdin, as already mentioned. This is true, however, only of small amounts of urobilinogen that under ordinary circumstances give but a weak (light-pink) reaction. In cases in which bilirubin or biliverdin might mask a weak reaction, the use of a spectroscope quickly determines the presence or absence of the characteristic urobilinogen-aldehyde band (maximum 565 millimicrons).

A number of substances exhibit yellow, red, or violet reactions with Ehrlich's reagent. These were discussed in detail by Naumann[102] with particular reference to the question of false-positive tests for urobilinogen. In my opinion, these various substances have relatively little practical significance. The color due to indol or skatol disappears when the test is carried out in the proper way with sodium acetate.[71, 101] I have not encountered false-positive tests due to other compounds with the exception of porphobilinogen,[103] a substance characteristic of acute porphyria[103, 104] and readily distinguished from urobilinogen by virtue of chloroform insolubility after forming the Ehrlich compound.[104]

Split Products of Hemoglobin or Bile Pigments

Pentdyopent. Prior to Bingold's studies,[21, 105–108] it was customary to believe that the degradation of hemoglobin in nature went no farther than bilirubin and urobilinogen — in other words, that although the porphyrin ring in the hemoglobin molecule was opened, the four pyrrol nuclei remained intact in a chain. Although this is undoubtedly correct for a major fraction of the destroyed hemoglobin, at least under ordinary circumstances,[1] Bingold's work has clearly revealed that both hemoglobin and the bile pigments may be split in vitro to substances with but two, rather than four, pyrrol nuclei. This transition undoubtedly occurs in vivo to an extent that is probably variable under different conditions.

Bingold has shown that blood freed of its catalase by heating is readily decolorized by hydrogen peroxide. Subsequent reduction with sodium hydrosulfite ($Na_2S_2O_4$) is then productive of a pink color with an absorption band that, in potassium hydroxide solution, has an absorption maximum at 525 millimicrons. Bingold simply employed this maximum as a descriptive name: "pentdyopent." In ammonia, the maximum absorption is at 540 millimicrons. This reaction has been shown by Fischer and his co-workers[109, 110] to be due to dipyrrylmethenes, which are undoubtedly formed during the above procedure by an oxidative splitting in half of the porphyrin ring in the hemoglobin or hemin molecule. As excreted in the urine, the dipyrrylmethene giving the pentdyopent reaction on addition of sodium hydrosulfite is colorless; in other words, it

is excreted as a "propentdyopent." Bingold obtained considerable evidence that the kidney is responsible for the formation of this substance. He noted that in hemoglobinuria the hemoglobin was decolorized by peroxide without preliminary heating, whereas in hematuria heating was necessary, just as it is with human blood. This difference was assumed to be due to removal of catalase by the kidney. Native propentdyopent was observed in urines from many and various pathologic states, but not under normal circumstances. It was found most frequently in urines containing bilirubin, and since the latter has been shown to give the pentdyopent reaction itself, the possibility exists that the main source of the propentdyopent is bile pigment rather than a direct oxidation of the hemoglobin. Bingold states specifically, however, that the reaction has been observed when bilirubin was absent. It should also be noted that urobilin IX *a* is readily converted to pentdyopent, whereas stercobilin is not.[109] Thus, it is quite conceivable that any urine sample containing mesobilirubinogen may also contain propentdyopent, if one assumes that a part of the former substance has been oxidized in the kidney.

The clinical significance of the pentdyopent group remains to be determined. Preliminary studies intended to provide a quantitative procedure have shown only that this will be attended with numerous and perhaps insurmountable difficulties, owing principally to the instability of the color. There is little doubt that the substance deserves further study, especially regarding its importance to the whole problem of hemoglobin metabolism. The main question to be answered is whether any appreciable fraction of the destroyed hemoglobin is ever excreted as propentdyopent. From time to time, a perplexing situation is encountered in which ordinary studies of blood destruction fail to reveal the fate of considerable amounts of hemoglobin.

In a twenty-eight-year-old patient with Hodgkin's disease, fever and severe anemia, the hemoglobin was 5.65 gm. per 100 cc. During the next nine days, 2400 cc. of blood (equivalent to 260 gm. hemoglobin) was given in nine separate transfusions, at the end of which time, the hemoglobin was 5.75 gm. per 100 cc. The F.U. averaged 515 mg. per day total excretion (equivalent to 167 gm. hemoglobin), and the urine showed small amounts of bilirubin and urobilinogen; in addition, urine pentdyopent tests, performed every other day, were positive. The fecal urobilinogen in the above case clearly indicated a hemolytic process, but failed to account for approximately 100 gm. of transfused hemoglobin. Although the blood volume was not determined, it is unlikely that it could have increased sufficiently to account for the discrepancy. In any event, the repeatedly positive pentdyopent reactions in such a case indicate the need for further study of this question.

Myobilin and mesobilifuscin. Until very recently, excretory products of muscle hemoglobin were unknown. Siedel and his co-workers[111, 112] have therefore opened a new field of investigation in their descriptions of a dipyrrylmethene isolated from the feces in certain conditions. Meldolesi, Siedel and Möller[112] first reported the excretion of a substance designated as "myobilin" in the feces of patients with progressive muscular dystrophy. This pigment was characterized by a brown color and a spontaneous green fluorescence (without zinc). The latter disappeared as the pigment was purified, and it was subsequently shown that the fluorescence was related to a combination of the pigment with protein. The substance was not detected in the urine, and it was thought that this was because the chromoprotein molecule was too large. No mention was made of its presence in the bile or of how the molecule was excreted by the liver. Interestingly enough, large amounts of the pigment were found in the feces of women during the first week of the puerperium, in whom it was thought that the pigment was derived from the myohemoglobin of the involuting uterus; in the patients with muscle atrophy or dystrophy, it was ascribed to the loss of hemoglobin from the voluntary muscle. The marked increase of myobilin in the feces was correlated directly with the hemoglobin-poor muscle.

After removal of the protein from the myobilin molecule, the underlying pigment was found to be a dipyrrylmethene, which was identified with mesobilifuscin, a substance that is dark brown, and does not fluoresce either spontaneously or with zinc; the zinc compound is relatively insoluble. The pigment could not be crystallized. These characteristics are entirely similar to those of the substance described several years ago under the name of "copronigrin," a brownish-black pigment obtained from the feces and characterized by an insoluble zinc compound.[54] It was recognized later that an entirely similar material could be obtained by oxidation of urobilin or stercobilin.[1] This is also quite in accord with the finding of Siedel et al.[112] that mesobilifuscin is present in the oxidized amorphous material (the so-called "*Körper II*") remaining after the reduction of bilirubin to mesobilirubinogen.

It is obvious that these newer studies raise many questions regarding not only the relatively unexplored field of myohemoglobin metabolism but also the whole problem of the bile pigments.

References

71. Watson, C. J. Studies of urobilinogen; an improved method for the quantitative estimation of urobilinogen in urine and feces. *Am. J. Clin. Path.* 6:458-475, 1936.
72. *Idem.* Studies of urobilinogen; urobilinogen in the urine and feces of subjects without evidence of disease of the liver or biliary tract. *Arch. Int. Med.* 59:196-205, 1937.
73. *Idem.* Studies of urobilinogen; the per diem excretion of urobilinogen in the common forms of jaundice and disease of the liver. *Arch. Int. Med.* 59:206-231, 1937.
74. Rich, A. R. The pathogenesis of the forms of jaundice. *Bull. Johns Hopkins Hosp.* 47:338-377, 1930.
75. Watson, C. J., and Bilden, E. Determination of urobilinogen in feces and in urine; comparison of Sparkman and Watson procedure. *Arch. Int. Med.* 68:740-746, 1941.
76. Watson, C. J. Hemolytic jaundice and macrocytic hemolytic anemia: certain observations in a series of 35 cases. *Ann. Int. Med.* 12:1782-1796, 1939.
77. Meulengracht, E. Icterus intermittens juvenilis (chronischer intermittierender juveniler Subikterus). *Klin. Wchnschr.* 18:118-121, 1939.
78. Rozendaal, H. M., Comfort, M. W., and Snell, A. M. Slight and latent jaundice; significance of elevated concentrations of bilirubin giving indirect van den Bergh reaction. *J. A. M. A.* 104:374-379, 1935.
79. Tecon, R. M. Les hyperbilirubinémies héréditaires: la cholémie familiale et l'ictère hémolytique. *Arch. d. mal. de l'app. digestif.* 28:567-589, 1938.
80. Dameshek, W., and Singer, K. Familial nonhemolytic jaundice; constitutional hepatic dysfunction with indirect van den Bergh reaction. *Arch. Int. Med.* 67:259-285, 1941.
81. Hiyeda, K. Experimentelle Studien über den Ikterus. Ein Beitrag zur Pathogenese des Stauungsikterus. *Beitr. z. path. Anat. u. z. allg. Path.* 73:541-565, 1925.
82. *Idem.* Experimentelle Studien über die Pathogenese des Ikterus. Über die Entstehung des Toluylendiaminikterus. *Beitr. z. path. Anat. u. z. allg. Path.* 78:389-407, 1927.
83. Ohno, Y. Experimentalstudien zur Ikterusgenese. *München. Med. Wchnschr.* 78:1639-1642, 1931.
84. Bloom, W. The rôle of the lymphatics in the absorption of bile pigment from the liver in early obstructive jaundice. *Bull. Johns Hopkins Hosp.* 34:316-320, 1923.
85. Watson, C. J. Regurgitation jaundice; clinical differentiation of the common forms with particular reference to the degree of biliary obstruction. *J. A. M. A.* 114:2427-2432, 1940.
86. Rous, P., and Drury, D. R. Jaundice as an expression of the physiological wastage of corpuscles. *J. Exper. Med.* 41:601-609, 1925.
87. Brule, M. Les ictères par choledocite. *Bull. méd. Paris* 52:217-221, 1938.
88. van den Bergh, A. A. H., and Kamerling, A. W. C. G. Levercirrhose met haemolytische anaemie en massale haematinaemie. *Nederl. Tijdschr. v. geneesk.* 78:4432, 1934.
89. Fairley, N. H. Methaemalbumin in man (pseudo-methaemoglobin). *Proc. Roy. Soc. Med.* 32:1278-1280, 1939.
90. Roholm, K., and Krarup, N. B. Die Histopathologie der Leber bei sog. Salvarsanikterus, mittels Aspirations biopsie untersucht. *Arch. f. Dermat. u. Syph.* 181:36, 1940.
91. Hanger, F. M., Jr., and Gutman, A. B. Postarsphenamine jaundice apparently due to obstruction of intrahepatic biliary tract. *J. A. M. A.* 115:263-271, 1940.
92. Watson, C. J., and Spink, W. W. Effect of sulfanilamide and sulfapyridine on hemoglobin metabolism and hepatic function. *Arch. Int. Med.* 65:825-846, 1940.
93. van den Bergh A. A. H. Der Gallenfarbstoff im Blute. Leiden: Van Doesburgh, 1928.
94. Edelman, M. H., Halpern, L., and Killian, J. A. Urobilinuria; its prognostic value in children with heart disease. *Am. J. Dis. Child.* 39:711-728, 1930.
95. Oliva, G., and Massimello, F. Retention of urobilin in nephritic patients. *Arch. per le sc. med.* 59:467-484, 1935.
96. Schiller, W. Zur Entstehung der Urobilinogenurie. *Wien. Arch. f. inn. Med.* 12:417-428, 1926.
97. White, F. W. The galactose tolerance and urobilinogen tests in the differential diagnosis of painless jaundice. *Am. J. Digest. Dis. & Nutrition* 4:315-325, 1937.
98. Wallace, G. B., and Diamond, J. S. Significance of urobilogen in the urine as a test for liver function with description of simple quantitative method for its estimation. *Arch. Int. Med.* 35:698-725, 1925.
99. White, F. W., Meiklejohn, A. P., Deutsch, E., and Kark, R. A comparison of three urobilinogen tests in the urine (Watson, Sparkman, and Wallace and Diamond methods), in jaundice and diseases of the liver. *Am. J. Digest. Dis. & Nutrition* 8:346-353, 1941.
100. Sparkman, R. Studies of urobilinogen; a simple and rapid method for quantitative determination of urobilinogen in stool and in urine; normal values for excretion of urobilinogen in single specimens in urine and stool; clinical value of determinations of urobilinogen content of single specimens of urine and stool. *Arch. Int. Med.* 63:858-883, 1939.
101. Terwen, A. J. L. Über ein neues Verfahren zur quantitativen Urobilinbestimmung in Harn und Stuhl und über die Bereitung und die Eigenschaften von einem möglichst reinen Urobilinpräparat. *Deutsch. Arch. f. klin. Med.* 149:72-101, 1925.
102. Naumann, H. N. The reaction of urobilinogen with p-dimethylaminobenzaldehyde. *J. Lab. & Clin. Med.* 23:1127-1132, 1938.
103. Waldenström, J. Studien über Porphyrie. *Acta med. Scandinav–Supp.* 82:1-254, 1937.
104. Watson, C. J., and Schwartz, S. A simple test for urinary porphobilinogen. *Proc. Soc. Exper. Biol. & Med.* 47:393, 1941.
105. Bingold, K. Die Niere als blutzerstörendes Organ. (Zur Physiologie des Blutstoffwechsels.) *Klin. Wchnschr.* 12:1201-1206, 1933.
106. *Idem.* Über die Bedeutung von Katalase und Hydroperoxyd für den Blutstoffwechsel. Darstellung eines biologischen Blutfarbstoffabbaues auf Grund von Modellversuchen. *Deutsches Arch. f. klin. Med.* 177:230-261, 1935.
107. *Idem.* Über das Schicksal des überalterten Blutfarbstoffes im Organismus. *Ztschr. f. d. ges. exper. Med.* 99:325-340, 1936.
108. *Idem.* Eigenschaften und physiologische Bedeutung des Pentdyopents. (Pentdyopent als Redoxsystem.) *Klin. Wchnschr.* 17:289-295, 1938.
109. Fischer, H., and Müller, A. Über die Pentdyopent-Reaktion. *Ztschr. f. physiol. Chem.* 246:43-58, 1937.
110. Fischer, H., and v. Dobeneck, H. F. Über die Pentdyopent-Reaktion. *Ztschr. f. physiol. Chem.* 263:125-146, 1940.
111. Siedel, W., and Möller, H. Über Mesobilifuscin, ein neues physiologisches Abbauprodukt des Häms bzw. Hämatins. I. Mitteil.: Konstitution und Teilsynthese. *Ztschr. f. physiol. Chem.* 259:113-136, 1939.
112. Meldolesi, G., Siedel, W., and Möller, H. Über Myobilin. *Ztschr. f. physiol. Chem.* 259:137-149, 1939.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28451

PRESENTATION OF CASE

A forty-two-year-old housewife was admitted to the hospital because of high blood pressure and a cough productive of small amounts of blood.

Four years prior to admission the patient had a "dizzy spell." Because of an elevation of blood pressure and increased hair about the face her physician sent her to another Boston hospital for adrenal studies. On admission at that hospital her blood pressure was 225 systolic, 150 diastolic. Periadrenal air insufflation studies and bilateral adrenal explorations were made. The adrenals were said to have been normal, and no ovarian tumors were felt. Owing to wound sepsis complicating the postoperative course, the patient was hospitalized for more than a month. At the time of discharge her blood pressure was 160 systolic, 110 diastolic. She soon became active again and remained so until one year prior to admission. At this time, after working rather hard in the garden, she began to cough up a "bloody sputum." At this time she noticed some blurring of vision. After approximately two weeks, these symptoms subsided and she seemed well. Two or three months before entry she developed exertional dyspnea and vision was again impaired, and six weeks before she had another episode similar to that noted a year previously; cough productive of bloody sputum continued to the time of admission. During this last attack, dyspnea became progressively worse and at times she noted "attacks of feeling as if there was a weight on the chest." During the week prior to admission there was mild ankle edema. She had been taking 1 tablet of digitalis each day during the six months before entry to this hospital.

The family history was noncontributory. There were two uncomplicated pregnancies eighteen and twelve years before entry.

Physical examination revealed a fairly well-nourished woman sitting up in bed and obviously making no attempt to minimize her discomfort. The skin seemed exceedingly thin and atrophic. The facial hair was noticeable but not heavy. Respirations were rapid but apparently not labored. There was questionable cyanosis of the lips. The neck veins were moderately distended. Both optic disks were blurred. There was a marked arteriovenous nicking, and there were several small flame-shaped areas of hemorrhage in the right fundus. The anteroposterior diameter of the chest was slightly increased. The left side seemed to lag a bit with inspiration. At the left base posteriorly there were dullness to percussion, absent tactile fremitus, decreased vocal fremitus and diminished breath sounds. These signs disappeared toward the axilla. Over the lower half of the right lung posteriorly there were a few coarse rales. The heart was moderately enlarged to percussion, and the sounds were of fairly good quality. No murmurs were audible. There was marked tenderness in the right upper quadrant. The liver edge could not definitely be felt, but dullness was percussed below the costal margin. There was moderate clubbing of the fingers — the patient indicated that her fingers had always had this shape and that her father's fingers had a similar shape. The examining physician added the note that on observing her raise the bloody material it did not seem to come from the lungs.

The blood pressure was 220 systolic, 140 diastolic. The temperature was 99.6°F., the pulse 90, and the respirations 25.

The examination of the blood revealed a red-cell count of 3,900,000, and white-cell count of 12,900 with 72 per cent polymorphonuclears. The hemoglobin was 60 per cent. The urine was alkaline in reaction, had a specific gravity of 1.010 and gave a +++ test for albumin; the sediment contained a rare red blood cell and a few white cells per high-power field. The blood Hinton test was negative. The blood nonprotein nitrogen was 40 mg. per 100 cc., and the serum protein 7.2 gm., with the albumin 2.2 gm. and the globulin 5.0 gm., making a 2.4 ratio. The van den Bergh test was normal. The prothrombin time was 30 seconds (normal, 25 seconds). The cephalin flocculation test was 0 at 24°C. and ± at 48°C. The fasting blood sugar was 145 mg. per 100 cc. The 17-ketosteroids excretion in the urine was 2.4 mg. every twenty-four hours. A urine culture revealed nonhemolytic streptococci. An electrocardiogram demonstrated a normal sinus rhythm with a rate of 86. The PR interval was 0.16 second. There were left-axis deviation, depression of the ST segment in Leads 2 and 4, and a diphasic low T wave in Leads 1 and 2. Repeated studies of the basal metabolism revealed rates ranging from +31 to +56 per cent.

An x-ray film of the chest showed spotty hazy areas of increased density throughout the midlung fields, more marked on the right side. There was a small amount of fluid at the right base, and a larger amount at the left costophrenic angle. The

aorta was calcified but not dilated. The heart was enlarged, chiefly in the region of the left ventricle. An intravenous pyelogram showed normal kidney outlines and poor dye excretion.

The patient was treated with digitalis and Mercupurin without much improvement. On the fifth day after admission, in preparation for a phenosulfonephthalein test, 1000 cc. of water was administered by mouth. This resulted in early anuria and later in dysuria. The next day, one hour following the administration of an evening sedative (3 gr. of Amytal), she became irrational and restless. Cheyne–Stokes respirations developed a half hour later. A stomach lavage stopped the irregular respirations, but two hours later these recurred. Ten cc. of aminophyllin was administered intravenously and permanently stopped the Cheyne–Stokes respirations.

Two days later she complained of severe back pain, which radiated to the left. The urine had a specific gravity of 1.020 and gave a +++ test for albumin and a ++++ test for diacetic acid, and the sediment contained 1 red cell and 1 white cell per high-power field. Catheterized specimens of urine examined on the succeeding days contained many red cells and occasional white cells. No casts were found. The blood chloride was 92.5 milliequiv., and the bicarbonate 26.0 milliequiv. per liter. At this time the temperature was slightly elevated, reaching an evening peak of 100°F., and she complained of generalized aches and pains. Another chest roentgenogram still showed the same findings. On the nineteenth day after admission the patient said she felt poorly and complained of some nausea. Three days later she suddenly collapsed and had generalized convulsions. These ceased in a few seconds. When seen by a physician she was cyanotic. The heart sounds were inaudible, but feeble gasping respirations were present. She died within three minutes of the observed onset of the attack.

Differential Diagnosis

Dr. Wyman Richardson: I might interpolate here that one would be anxious to know whether these clubbed fingers showed a softening at the base of the nail, so that when you pressed them the nailbed seemed to be slightly afloat, because I do not believe you ever see that in congenitally clubbed fingers. I am going to disregard this finding.

The blood was slightly hypochromic, which probably is not significant.

I should like to see the chest plates.

Dr. George W. Holmes: The films cover a period of a little over a month. One film of the chest was taken in June, and the others in July. It is obvious that there is a lesion in the chest. The process is at the base of the lung, more on the right than on the left. It is accompanied by a moderate enlargement of the heart, chiefly to the left in the region of the ventricle. This second film was taken with a Bucky diaphragm and overexposure to bring out the character of this process in the lower part of the chest. I think the bronchial shadows are enlarged. In other words, this looks like a bronchiectasis so far as the chest films go. I do not see any definite evidence of fluid. My interpretation may be wrong, but that is the first thing I should think of.

Dr. Richardson: How about congestion due to cardiac failure?

Dr. Holmes: I should not think so. In the first place, the heart does not have the shape seen in cardiac failure. There is some dilatation, but it does not look like a failing heart. The auricles are not dilated enough to account for the change in the lung fields.

Dr. Richardson: It is not the condition of localized edema associated with renal failure that we have been shown by Drs. Schatzki and Scott?*

Dr. Holmes: It does not look like it to me.

Dr. Richardson: I was caught on that before.

Dr. Holmes: There is such a thing; I cannot say that it is not present, but my impression is that it is not. In the films taken of the abdomen, the kidney outlines are quite evident on both sides and the right kidney is distinctly larger than the left but both of them, I think, are within normal limits. Such a slight difference in size would not mean anything definitely abnormal.

Dr. Richardson: Supposing you were thinking in terms of myeloma kidney, do you see anything suggestive there?

Dr. Holmes: I should expect them both to be enlarged in that case. The most likely interpretation of the kidneys is that the right was not functioning well and that the left kidney had undergone compensatory hypertrophy. The liver shadow is well seen, and this, I think, is the spleen. If it is spleen, there is no definite enlargement, nor do I think that the liver is enlarged.

Dr. Richardson: But you would not say that it was small?

Dr. Holmes: No. Of course, x-ray evidence of change in the size of the spleen is not accurate. But I certainly should not interpret that as being particularly abnormal.

So far as the excretion of the dye is concerned, it is very poor. If the test was carried out properly, I think we can interpret this as evidence of poor function in the kidney.

*Schatzki, R., and Scott, A. T. Unpublished data.

DR. RICHARDSON: How about the bone structure?

DR. HOLMES: It is well within normal limits; I do not see any decalcification or any other change.

DR. RICHARDSON: They did not do the skull?

DR. HOLMES: No.

DR. RICHARDSON: In the first place I am going to try to lay this endocrine ghost that has been stalking around through this whole story. It is not clear why they operated on the adrenal glands at the other hospital, whether to look for an adrenal medullary tumor, a so-called "pheochromocytoma," or whether to look for an adrenal cortex tumor. If you glance through the record for evidence of endocrine difficulty you find it but it all points in different directions. In the first place, she had two uncomplicated pregnancies. The menstrual history is not mentioned; with the history of normal pregnancy we probably can consider it normal. We are not sure whether she was amenorrheic at the time of entry. I think facial hair that is noticeable but not heavy is not to be overemphasized. It is a common hereditary characteristic. Thin and atrophic skin may suggest an overactive anterior pituitary gland. The laboratory finding of decreased 17-ketosteroid excretion is absolutely opposed to an adrenocortical tumor and in the opposite direction from the increased basal metabolic rate. I cannot see how one can talk about Cushing's syndrome in this case by any stretch of the imagination just because she has a little hair, hypertension and slight anemia. I cannot explain, incidentally, the lowered ketosteroid excretion by any theory. I do not know much about endocrine disease, but I will say that I doubt that Dr. Mallory will find any very striking primary disease involving the endocrine glands.

There are two ways of attacking this problem, one from a purely clinical angle and the other from the laboratory findings. If I take the clinical angle alone, I think this patient had hypertensive heart disease, cardiac failure and renal failure, probably secondary to renal congestion; and the manner of death, although rather sudden with convulsions, is best explained on the basis of cardiac failure or some vascular difficulty. If I look at the laboratory side of it, I am going to get into trouble. She had a mild anemia, possibly accountable on the basis of some renal failure and her general condition. Then there was this serum protein of 7.2 gm. per 100 cc., which is on the high side of normal, particularly since the normal values have recently been running about 6 gm. or a little over. At any rate, the globulin is markedly and definitely increased. One cannot take too seriously any single laboratory finding, but I think one has to take this seriously. When I try to figure out what diseases produce increased globulin to this extent, there are not many that I have to mention. Certainly not cholera or lymphogranuloma inguinale; and I do not believe that sarcoid would kill the patient. I come down to two causes that seem likely — multiple myeloma and some disease of the liver like cirrhosis.

I get all balled up with electrocardiograms, but I do not see anything specific here. I shall ask Dr. Harwood to give an opinion, but before he says anything, I shall say that the tracing is consistent with hypertensive heart disease and failure.

DR. REED HARWOOD: I agree.

DR. RICHARDSON: Dr. Holmes bothers me by not being willing to say that the x-ray findings might be related to cardiac failure.

DR. HOLMES: I should not say that they could not be. On the other hand, I think they are less likely to be that than something else.

DR. RICHARDSON: Regarding the clubbed fingers, I remember a recent case in which they were very important in connection with bacterial endocarditis, but I cannot see that this case hooks up in any way with bacterial endocarditis. I considered the question of periarteritis nodosa or some similar vascular disease, but I do not see any point in talking about that without more definite evidence. You can have renal and vascular changes in periarteritis nodosa, but not necessarily hypertension and usually more fever. In this case the whole story does not seem to me to fit that sort of disease. So that I have come down rather reluctantly to two diagnoses. One is hypertensive heart disease, with some question in regard to what the kidneys might show, — probably congestion of the kidney with failure and rather fine vascular changes, — with perhaps some vascular changes in the brain, possibly small areas of hemorrhage, and with cirrhosis of the liver on some basis either entirely incidental or possibly the "rare bird" that I almost never see and talk too much about — cardiac cirrhosis. That is one possibility. The only other thing I can do is to say that this patient had a plasma-cell myeloma with myeloma nephrosis, renal failure, hypertension on this basis and the train of symptoms following hypertension with combined renal and cardiac failure. I have not seen many of these cases, but to me they showed renal failure much more clearly than this patient showed. The only things in favor of it are the high globulin, the poor renal excretion of dye and the albuminuria. Bence-Jones protein was not looked for. Since I put myself on the horns

of that dilemma, the obvious thing to do is to take the common disease, and I am going to say that this patient's difficulty was routine hypertension resulting in cardiac failure and mild renal failure, largely on a congestive basis, with vascular changes in the kidneys and cirrhosis of the liver (? "cardiac").

Dr. Tracy B. Mallory: I should like to ask Dr. Holmes if in the last film he can see anything in the superior mediastinum.

Dr. Holmes: I can see something in the last film that is not in the first. It is beneath the clavicle on the right side. It did not impress me.

Dr. Mallory: You do not care to go farther?

Dr. Holmes: Recently we have seen a series of cases with shadows of that kind, which turned out to be due to the innominate artery. Most of them are normal. They are usually caused by tortuosity of the aorta. Aneurysm of the innominate artery, however, can produce such a shadow, as can a large peritracheal lymph node.

Clinical Diagnoses

Hypertension.
Hypertensive and coronary heart disease.
Coronary occlusion.

Dr. Richardson's Diagnoses

Hypertension.
Hypertensive heart disease.
Congestive failure.
Vascular nephritis (slight).
Cirrhosis of the liver (? "cardiac").

Anatomical Diagnoses

Dissecting aneurysm of aorta, with rupture into mediastinum and left pleural cavity.
Hematoma, left.
Hypertrophy of heart, hypertensive type.
Arteriosclerosis, marked: aorta.
Pyelonephritis, chronic, inactive.
Cystitis, acute.

Pathological Discussion

Dr. Mallory: When this patient first came in, she obviously impressed everyone who saw her as the complaining sort. Consequently from then on when she had discomfort they discounted it heavily. She did complain bitterly of pain in the back, and the note in the record reads, "Patient complains of pain in the back, probably postural." Nothing was done about it. In another note, it is stated that she complained of aches and pains all over but apparently no specific inquiries were made as to where they might or might not be. That is unfortunate because she unquestionably did have severe pain in the back, owing to a dissecting aneurysm. The dissection had evidently occurred some time before death. The day on which she complained of severe back pain was fourteen days before death, and the blood in the outer channel was not merely clotted but partially organized. It was also evident that at the time of or immediately following the initial attack of dissection the outer wall had torn slightly; this resulted in a leakage of blood into the superior mediastinum, where a hematoma of considerable dimensions was present, which likewise showed organization. This must have been present at the time the last chest film was taken.

The terminal episode in this patient was a further rupture of the outer layer into the mediastinum and hence into the left pleural cavity, which contained 2500 cc. of fresh blood.

The kidneys were interesting. They were somewhat small, weighing 250 gm., but markedly scarred, and both showed an extremely severe vascular disease with disproportionate destruction of the tubules as compared with that of the glomeruli. Whether it was entirely a vascular nephritis or whether there was an underlying old pyelonephritis, I am not certain. I am tempted to believe this was hypertension based on a long-standing and inactive pyelonephritis.

The terminal changes in the urine, — the occurrence of numbers of red cells and so forth, — I think was not due to any interference with their blood supply by the dissecting aneurysm but rather to the development of acute hemorrhagic cystitis, which was merely a terminal complication.

The liver showed a very mild chronic type of congestion and by no stretch of the imagination could you call it "cardiac cirrhosis." The bone marrow showed no plasma cells. The lungs showed a little emphysema and fibrosis, so the pulmonary changes were not entirely due to congestive failure. We did not find any clearly defined bronchiectatic cavities, however, so I am left with absolutely no explanation of the elevated globulin and reversed albumin-globulin ratio. We found no evidence of endocrinopathy; the pituitary, thyroid and adrenal glands and the ovaries were all quite normal.

CASE 28452

Presentation of Case

First admission. A fifty-eight-year-old physician was admitted because of diarrhea and pain in the right lower quadrant.

For fifteen years prior to admission the patient stated that he tended to have frequent episodes of diarrhea approximately every two or three weeks, each lasting two or three days. These

were usually accompanied by gaseous eructations and sometimes by a spell of vomiting. Occasionally there was a coincident fever. Hypogastric cramps occasionally accompanied the diarrhea, and often these were localized in the right lower quadrant. There was some mucus in the stools, but they were never tarry and did not contain blood.

In addition to the fairly mild episodes in which he had three or four loose movements each day, he had two acute attacks, one six years and another eight weeks before entry, in which he was prostrated by acute abdominal cramps, nausea, vomiting, very frequent watery stools, fever and an initial chill. The most recent episode began about twenty hours before admission when, following a hearty dinner, he began to have watery stools, vomited, retched several times and had generalized abdominal cramps. There was apparently no fever. He had a miserable night but felt better the next morning. During the next day he had two formed stools but later in the afternoon he had a shaking chill. His physician reported that his temperature was 103°F. There was no further diarrhea. The patient believed that oranges or pineapple juice, onions, and fresh fruits in general upset him and initiated the diarrhea. There was no weight loss.

The family history was noncontributory.

The patient had had a severe attack of scarlet fever at the age of fourteen, followed by nephritis, which later went into a nephrotic stage with persistent albuminuria for more than twenty years. He believed that he had had no albuminuria during the subsequent twenty-two years. He had taken several trips to the West Indies within the previous ten years, and on one occasion had had an attack of diarrhea that lasted only one night. Four years before entry, he had an attack of severe substernal pain after walking four blocks. This lasted five minutes and never recurred. Eight weeks previously, during the attack of diarrhea, his heart rate jumped to 180 but returned to a normal rate after pressure was applied to the carotid sinus. He had been taking some alkali in recent months for gaseous eructations and "heart burn."

Physical examination revealed a slightly flushed, obese man in some discomfort. The examination of the heart and lungs was negative except for scattered fine moist rales audible over the posterior bases of both lungs. The abdomen was soft and protuberant. There was no rigidity, and no masses were felt. There was a slight amount of tenderness over most of the right lower quadrant. No costovertebral tenderness could be elicited. The peristaltic sounds were hyperactive. No tenderness was found on rectal examination, and the prostate was not enlarged.

The blood pressure was 142 systolic, 82 diastolic. The temperature was 98°F., the pulse 110, and the respirations 20.

The examination of the blood revealed a hemoglobin of 14.7 gm. and a white-cell count of 14,100 with 92 per cent polymorphonuclears, 6 per cent lymphocytes and 2 per cent monocytes. Twenty-four hours later the white-cell count had dropped to 11,400 with 71 per cent polymorphonuclears. Further white-cell counts showed figures consistently less than this. A blood Hinton test was negative, as was the urine examination. The blood nonprotein nitrogen was 22 mg. per 100 cc. The stool was greenish brown and guaiac negative; no amebas or amebic cysts were seen. An electrocardiogram demonstrated a normal sinus rhythm of 100 and slightly lowered T waves.

A flat plate of the abdomen showed what was interpreted as tuberculous lymph nodes in the right lower quadrant. There were no abnormal gas or soft-tissue shadows. The kidney outlines were normal. There were no shadows present that could be interpreted as stones. A barium enema showed that the colon filled readily; there were no constant irregularities or filling defects. About 15 cm. of the terminal ileum filled, and there was a constriction in its terminal portion opposite the tip of the cecum. The appendix was not visible. Practically all the barium was evacuated. Later a barium meal revealed a small hiatus hernia and fairly persistent spasm of the antrum of the stomach and the pyloric valve. The stomach and duodenum were otherwise normal. Serial examinations of the small bowel revealed no evidence of obstruction, but the constriction in the terminal ileum was again demonstrated. The mucosa at the site of the constriction was distorted and appeared to have been destroyed over an area less than 1.0 cm. in length. The cecum did not remain filled completely, there being a gap between the terminal ileum and transverse colon producing the so-called "Stierlin sign." The mucosa of the cecum and ileum appeared normal. The appendix did not fill. There was no dilatation of the small bowel.

The stools were repeatedly examined for the presence of amebas and amebic cysts, employing the zinc sulfate flotation method, but without success.

After nine days of hospitalization the patient was discharged without an established diagnosis. He was told to return after a month of rest for an exploratory abdominal operation.

Second admission (one month later). Following discharge the patient had felt well. During

the interval he had not suffered with tenesmus, cramps or diarrhea.

There was no definite change in the physical examination, and on the second day an operation was performed.

Differential Diagnosis

Dr. Clifford Franseen: This case, in summary, resolves itself into the differential diagnosis of lesions of the terminal ileum that are chronic and produce partial intestinal obstruction or perhaps chronic or recurring intussusception in a man of fifty-eight. Except for the findings in the right lower quadrant, the data do not seem to be relevant. The history, of course, is important, especially the fifteen-year duration, if one is going to try to make a single diagnosis that will explain the symptoms over all these years. Throughout this period he had recurrent inflammatory episodes and obstruction, cramps, nausea, vomiting, watery stools and so forth. One must depend on the x-ray findings in the right lower quadrant because he had no palpable mass.

The diagnoses to be considered are several. The first thing that suggests itself from the x-ray findings is tuberculous nodes in the right lower quadrant. Presumably the record means that calcified nodes were found. These can occur coincidentally in a large number of people of this age in x-ray examinations for other conditions, and alone they do not establish the diagnosis. Similarly, the appendix did not fill. In a large percentage of patients of this age who have routine examinations, I am quite sure the appendix does not fill, and it may not be important in this case.

I wonder if we may see the x-rays before we go any farther.

Dr. Richard Schatzki: This is the barium enema, and this represents the small area of narrowing that is described in the record. It is about 1.5 to 2.0 cm. in length and is constant because the film taken after evacuation also shows it. I should agree with the record that the mucosal pattern is markedly distorted and that the mucosa seems to be destroyed. This is another set of films taken after the oral administration of barium, and you can see this same area again. It is certainly a well-localized destruction of the ileum.

Dr. Franseen: Would you care to say a word about Stierlin's sign?

Dr. Schatzki: I think what the examiner meant is what a Swiss roentgenologist described thirty years ago — namely, a constant failure of the cecum and of the adjacent part of the ascending colon to fill during barium examination by mouth, in association with tuberculosis of the ileocecal region. I should say this was suspicious of it but by no means definite.

Dr. Franseen: This could be present in any condition that gives spasm of the cecum?

Dr. Schatzki: Very definitely so. The record does not say anything about the cecum, but it appears normal so far as I can see.

Dr. Franseen: Is that area at the lower end of the cecum significant? It does not show the same smooth outline as the rest.

Dr. Schatzki: It looks quite normal on the postevacuation film, however.

Dr. Franseen: To go back to the things we have to consider. First, we have tuberculosis. Are these the calcified areas here?

Dr. Schatzki: Yes.

Dr. Franseen: They are calcified retroperitoneal nodes. If one considers a tuberculous process that has gone on over a period of fifteen years, it seems to me that one would expect to find more than is seen here. This lesion appears primarily to involve the ileum, over a relatively short segment, and not the cecum. After fifteen years one would have expected an inactive process, probably a cicatrizing lesion, which might simulate this condition.

I am trying to recall an interesting case in a man somewhere around fifty years of age that we had three or four years ago. The only lesion he had was a minute constricting area some distance from the ileocecal valve. If I had not known of that case I should not be suspicious of this area as being due to tuberculosis. It is my impression that tuberculosis is primarily an ulcerating process and would occur most likely in a younger man.

The next thing to consider, of course, is regional enteritis. It, too, is a disease of youth. I personally do not remember any case in a patient as old as this man, nor do several of my colleagues whom I questioned. Regional enteritis usually occurs in patients under forty. It is primarily a disease of youth, and probably of not so long duration as this condition, which has gone on for fifteen years. It also seems likely that if it had gone on to this stage of intestinal obstruction a mass would have been found, which is not true. Furthermore, the typical x-ray appearance of the bowel with the usual string sign is not present. The last patient I saw who had the string sign was a man of forty who proved to have an adenocarcinoma, so that sign may also be misleading. I should not consider regional enteritis seriously for these reasons.

Other inflammatory processes must be discussed because there were recurrent episodes. An appendix abscess sometimes produces bizarre findings, but under this diagnosis one would have to

make some other explanation for the episodes preceding the present one unless the patient had an obscure chronic appendicitis associated with obstruction. Also, no mass was palpable, so that there is not much reason to consider appendix abscess in this case.

One must, of course, consider a tumor. The malignant tumors that perhaps most frequently involve this segment of the bowel are sarcomas of the small intestine, carcinomas and lymphosarcomas. Lymphosarcoma would probably involve a larger area. The long duration is against malignancy unless it had been superimposed on a benign condition over these years. One might consider that the repeated episodes of obstruction were caused by intermittent intussusception or partial intestinal obstruction by some benign tumor in this region, but the usual benign tumors, such as lipomas, xanthomas and fibromas, are ordinarily somewhat pedunculated and are not circular and constricting as this lesion appears to be. The only other condition that I can consider in which one could have a benign tumor which would gradually advance and produce this picture is a carcinoid. The small intestine is the commonest site of carcinoid, except the appendix. In this case, one might suppose that the appendix was the primary site of the carcinoid and that the area in the ileum was involved secondarily, but I think that a primary carcinoid of the ileum is more probable. That would fit in best with the history of fifteen years' duration, because these tumors grow very slowly; however, I do not know of any case of carcinoid with such a long duration. It is conceivable that it might occur because other similar benign conditions can go on and produce symptoms like these until the final episode of more complete obstruction. The patient was in the age group in which carcinoid commonly occurs—another point in its favor. Likewise, the mass was small. Carcinoids can, of course, grow to considerable size and metastasize.

I should have to use carcinoid of the ileum as the diagnosis best fitted to this case. Tuberculosis cannot be entirely excluded, but I think it is unlikely.

Dr. Schatzki: If our impression is correct that the mucosa was destroyed, does that not argue against the diagnosis of carcinoid?

Dr. Franseen: Yes; but that is at variance with the opinion given in the abstract. It says that the area was possibly destroyed over an area 1 cm. in length, which would be consistent with carcinoid. Of course, if the carcinoid had become malignant, the destruction of the mucosa would be consistent.

Dr. Schatzki: I do not know the answer, but I should say from looking at the films that the mucosa was destroyed.

Dr. Franseen: That would be very much more in favor of a malignant process, possibly carcinoma.

Dr. Mallory: Even in cases in which carcinoids have become invasive and have metastasized to the regional lymph nodes we have not seen even one case with ulceration in the mucosa. It grows in a disk-like form in the submucosa and never spreads through to the surface.

Dr. Franseen: But when carcinoma intervenes, what occurs?

Dr. Mallory: That does not happen. A carcinoid is not an epithelial tumor and never turns into carcinoma. It is potentially a malignant tumor in its own right but does not become a carcinoma: it remains an argentaffine tumor.

Dr. Franseen: I understand that is a disputed point among pathologists. You believe that it does not become carcinomatous?

Dr. Mallory: Yes; Masson showed very definitely that it is a tumor of some peculiar nerve end organ rather than a tumor of the epithelium.

Clinical Diagnosis

Regional enteritis?
Tuberculosis?
Appendix abscess?

Dr. Franseen's Diagnosis

Carcinoid of ileum, probably malignant.

Anatomical Diagnoses

Appendicitis, healing.
Inflammation of Meckel's diverticulum, acute.

Pathological Discussion

Dr. Mallory: I am sorry Dr. Arthur W. Allen, who operated on this patient, is not here to discuss the case. On the first entry, the patient was studied by Dr. Allen and Dr. Chester M. Jones and was discharged with three questionable diagnoses: regional enteritis, tuberculosis and appendix abscess. It was eventually decided that the possibility of appendix abscess was great enough so that he should return for operation as soon as he could adjust his affairs, and that was done.

On the second entry he was promptly operated on, and the first thing that popped into sight when the abdomen was opened was a Meckel's diverticulum. A little further exploration showed an appendix buried in adhesions along the brim of the pelvis, with no pus about it and no evidence of abscess. Both the appendix and the Meckel's diverticulum were removed. The surgeon's impression was that the appendix had been recently inflamed and was in a subsiding stage. In the laboratory, we formed another impression.

The appendix did not impress us greatly, and the Meckel's diverticulum contained purulent exudate in the lumen. So we believed there was an acute or still active diverticulitis and that the appendix, which was about two thirds obliterated, had undoubtedly, at various times in the past, been the seat of an inflammatory process but probably not in an extremely recent period. The anatomic findings are difficult to correlate with the x-ray findings, and yet I think we must assume that Dr. Allen was able to rule out such possibilities as tuberculosis, regional ileitis and carcinoid since he had a good exposure of the entire terminal ileum and nothing was found except the Meckel's diverticulum.

DR. SCHATZKI: How far away from the ileocecal valve was the Meckel's diverticulum?

DR. MALLORY: I judge very close, but it was not measured.

DR. SCHATZKI: This lesion is only 5 cm. proximal to the ileocecal valve. That would be very low for a Meckel's diverticulum. Furthermore, I still cannot see a diverticulum.

DR. GLENDY: How often can you demonstrate it?

DR. SCHATZKI: We hardly ever see the diverticulum itself, probably because it looks so much like the intestine. This is particularly true in the usual position of a diverticulum, higher up where it is difficult to distinguish the intestinal loops. But in this case the questionable loop is clearly separated. The diverticulum should have shown up, unless its entrance was closed and therefore did not fill with barium.

DR. MALLORY: The operative note said that the walls about the mouth were very thick.

DR. SCHATZKI: Then that is a possibility; however, the position is unusually low for a Meckel's diverticulum.

DR. GLENDY: Do you think that the diverticulum was close enough to the area of narrowing to produce spasm?

DR. MALLORY: That is my hypothesis. I think anyone has a right to disagree with it. I do not believe we have proved it at all.

DR. FRANSEEN: Spasm could not produce destruction of the mucosa.

DR. SCHATZKI: Obviously, the mucosa was not destroyed, just swollen.

* * *

The following post-conference statement was obtained from Dr. Arthur W. Allen:

I regret having been absent from the clinicopathological conference on Case 28452, because I could have cleared up many of the points that seemed to worry the discussers.

In the first place the patient gave a very atypical story for appendicitis, since in addition to nausea, vomiting and abdominal pain he had profuse diarrhea. This is very unusual in appendicitis because the inflamed appendix usually does not rest near enough to the rectum to produce peristalsis by irritation.

The patient entered the hospital twenty hours after the onset of his episode, and although he had a leukocytosis consistent with an inflammatory process, the abdomen was generally tender and there was no evidence of localization, either abdominally or by rectal examination. Finally, however, he did develop tenderness in the right lower quadrant.

The probability that the condition was due to appendicitis was so strongly considered that the patient was strictly Ochsnerized, and he made a fairly prompt response to this treatment. His temperature, having reached 103°F. as a peak, came down to normal on the fourth day. Peristalsis, which had ceased after he entered the hospital, again became normal, and food and fluids were resumed by mouth.

The repeated minor episodes, with two previous severe attacks, always associated with a very sensitive colon, made us wonder whether the whole process might be accounted for on some basis other than simple, acute appendicitis. Very careful studies were made, including many stool examinations for amebas, since his first severe episode had taken place while on a Caribbean cruise.

The x-ray examinations were not quite so puzzling to Dr. Hampton and to me as they appeared to be at the time of the conference. In fact, Dr. Hampton thought that appendix abscess explained the situation better than any other diagnosis. After the febrile reaction had quieted down, there was a very definite, although ill-defined, mass which could be felt bimanually in the right side of the abdomen; and the patient was discharged with a diagnosis of appendicitis with peritonitis, to return for deliberate appendectomy after four weeks.

The findings at operation are not described well in the abstract, owing, I am sure, to our own carelessness in dictating the operative note. The Meckel's diverticulum was not adherent to any structure; it had no appearance whatever of acute inflammation, and the fact that it was found acutely inflamed by pathological examination does not indicate that this had anything to do with the acute episode six weeks previously. The appendix, however, was lying in the pelvis next to the rectum and was adherent to it, and when it was elevated out of the pelvis, it was obvious that we were freeing fresh, more recent adhesions. The distal half of the appendix was thickened and reddened, and appeared exactly like many I have removed several weeks after a known acute inflammatory attack.

There was no doubt whatever in my mind or in my assistant's mind that the appendix had accounted for the patient's acute attack and that the Meckel's diverticulum was, in fact, an incidental finding.

The patient's convalescence after operation was identical with the type that goes with an appendix removed under these circumstances; in other words, there was more febrile reaction than in the removal of an interval or normal appendix, and considerably more ileus than is usually seen. This might have been due to the added removal of the Meckel's diverticulum, but I believe is more likely to have been due to the stirring up of the quiescent infection in the pelvis.

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established in 1828

Owned by the Massachusetts Medical Society and Published under the Jurisdiction of the Committee on Publications

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society

Editorial Board

Joseph Garland, M.D. — Stephen Rushmore, M.D.
George R. Minot, M.D. — Henry R. Viets, M.D.
Frank H. Lahey, M.D. — Robert M. Green, M.D.
Shields Warren, M.D. — Charles C. Lund, M.D.
George L. Tobey, Jr., M.D. — John F. Fulton, M.D.
C. Guy Lane, M.D. — A. Warren Stearns, M.D.
William A. Rogers, M.D. — Dwight O'Hara, M.D.
Chester S. Keefer, M.D.

Associate Editors

Thomas H. Lanman, M.D. — Donald Munro, M.D.
Henry Jackson, Jr., M.D.

Walter P. Bowers, M.D., Editor Emeritus
Robert N. Nye, M.D., Managing Editor
Clara D. Davies, Assistant Editor

Subscription Terms: $6.00 per year in advance, postage paid, for the United States (medical students, $3.50 per year); Canada, $7.04 per year, Boston funds; $8.52 per year for all foreign countries belonging to the Postal Union.

Material for early publication should be received not later than noon on Friday.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston, Massachusetts.

THE ONE-DAY CURE FOR SYPHILIS

It is surprising that the *Reader's Digest*, which renders a notable service with its excellent summaries of current magazine articles and new books, should publish for lay consumption an article* on a new one-day cure for syphilis as if the procedure were already available for every physician to use as safe and scientific on any and all patients with syphilis.

Such an ill-advised statement has raised many false hopes and disturbed many patients who are progressing satisfactorily under treatment. It has instigated many queries to physicians and medical journals about a method that is still in the experimental stages. The method has very definite hazards. Not everyone can tolerate a fever of 106°F., and patients with certain defects should never be exposed to such a temperature. The apparatus and controls are not at hand. Neither physicians nor nurses have had sufficient training in the method. Too few cases have been treated and too short a time has elapsed to know if there are any late serious effects of the treatment and if the results on the disease are permanent. It may be a step forward in the treatment of syphilis, but much experimental work must be done to be sure that this particular technic is the proper procedure for every case of syphilis. There are many pitfalls in this complicated program, and it is cruel for a scientifically trained writer to propose such a method to the public as accepted and readily available in every city and town. Furthermore, why did this writer pick out an eleven-year-old article to stress the bad effects of routine antisyphilitic treatment? In a letter published in the September 19 issue of the *Journal of the American Medical Association*, Dr. Harold N. Cole, a distinguished syphilographer and the author of the former article, emphasizes the bad effects of publicizing prematurely an experimental procedure that needs confirmation before it is widely available for syphilis in general.

Physicians can assure their questioning patients that the one-day treatment is in the experimental stage and is not a safe and sure procedure and that it will eventually be made readily available if scientific evidence warrants its acceptance. Incidentally, one cannot refrain from suggesting that the publication of medical articles in a periodical for lay consumption is a great responsibility and one that cannot be discharged properly without the aid of competent medical opinion.

*de Kruif, P. Found: a one-day cure for syphilis. *Reader's Digest*, September, 1942.

GUIDES TO THERAPY FOR MEDICAL OFFICERS

An excellent pocket-sized technical manual, entitled *Guides to Therapy for Medical Officers*,† has recently been issued by the War Department. As

†War Department. Technical Manual 8-210. *Guides to Therapy for Medical Officers*. 185 pp. Washington: Government Printing Office, 1942.

stated in the opening paragraph, the purpose of this manual is to provide the medical officer with a handy text containing guides to therapy under emergency conditions or in diseases with which he is relatively unfamiliar. The accepted treatment of the diseases commonly encountered in civilian life is not discussed, nor are such topics as the control of communicable diseases and sanitation. In other words, it is intended to serve as a guide to the "general practitioners" of the Army and not as a text for specialists, who are likely to be stationed with evacuation units or in general hospitals. It is also emphasized that the text does not comprise rules and regulations that must be followed, but merely suggestions to be used at the discretion of the medical officer.

The manual is well conceived and carefully executed. The Surgeons General of the Army and Navy, early in 1940, requested the Division of Medical Sciences of the National Research Council to establish committees that should act in an advisory capacity to the two medical corps. Much of the text of this manual is based on material compiled by these committees. Final revision was conducted by pertinent divisions of the Office of the Surgeon General, United States Army. The manual was edited by a member of the Committee on Information of the National Research Council.

The reports of the many experts are presented in an easily readable, compact and orderly fashion. The major subjects covered are as follows: surgical emergencies; medical emergencies; diagnosis and treatment of venereal diseases; chemotherapy and serotherapy in certain infectious diseases; treatment and control of certain tropical diseases; and rickettsial diseases. The contributors to each of these sections include many of the leading names in American medicine and surgery.

Under surgical emergencies are included the commonest types of wounds in various parts of the body, the management of shock and the early treatment of burns. Most of the essential details are given, but the specialized forms of treatment that can be undertaken only by experts are almost entirely omitted. The section on medical emergencies covers the majority of situations that might arise under the great variety of conditions to which troops are likely to be subjected, including such diverse items as acute poisoning from various foods, chemicals, plants and animal sources, seasickness, altitude sickness, the effects of exposure to heat and cold, starvation and the acute psychoses. The sections on tropical and rickettsial disease are meant to acquaint medical officers with conditions that are rarely encountered in civilian practice but that are very likely to be met with in the far-flung regions where troops may be operating. Each section is preceded by a table of contents, and there is a well-arranged and easily usable index at the end of the volume.

The manual seems well suited for the purposes for which it is intended. In fact, it could advantageously serve as an abbreviated and handy text for general practitioners and for medical students and hospital interns who are likely to see active military service in the near future. It is likewise suitable as a "procedure book" for use in the emergency rooms of general hospitals. No doubt, the manual will be kept up to date when reprinting becomes necessary. It can be obtained for twenty-five cents from the Superintendent of Documents, Washington, D. C.

MEDICAL EPONYM

Schick Test

This was first described by Dr. Béla Schick (1877), then private docent in the clinic of Professor von Pirquet in Vienna, in an article "Die Diphtherietoxin-Hautreaktion des Menschen als Vorprobe der prophylaktischen Diphtherieheilseruminjektion [The Diphtheria-Toxin Skin Reaction in Man as a Preliminary Test in the Prophylactic Injection of Diphtheria Antitoxin]" in the *Münchener medizinische Wochenschrift* (60²:2608-2610, 1913). A portion of the translation follows:

> For intracutaneous injection, the ordinary 1-cc. Rekord syringe marked in tenths is needed. The most important part is the needle, which . . . should be as fine as possible, with a short bevel, in order that the opening of the needle may be covered as quickly as possible when it is introduced into the most superficial layers of the skin. A dose of 0.1 cc. of a dilution of the toxin, which must be calculated in each case, is

given. As a rule, one fiftieth of the minimal lethal dose for a 250-gram guinea pig suffices — for example, with a lethal dose of 0.005 cc. for a 250-gram guinea pig, an injection of 0.1 cc. of a 1:1000 dilution. If the injection is successful, there is at once apparent a white wheal-like elevation with dots corresponding to the orifices of the hair follicles.

The changes that occur at the site of injection of the diphtheria toxin resemble in appearance those occurring during the first twenty-four to forty-eight hours of a positive tuberculin reaction. . . .

A negative response to the intracutaneous test always indicates the presence of diphtheria-toxin antibodies in sufficient amounts for prophylaxis. . . . A positive test does not indicate their absence with the same certainty, since many individuals, children as well as adults, may show an inflammatory reaction at the site of injection of diphtheria toxin in spite of the presence of protective substances in their serums.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Analysis of Causes of Maternal Death in Massachusetts during 1941

Pneumonia

As the tabulation of medical causes of maternal death printed in last week's issue of the *Journal* shows, pneumonia ranked second to heart disease as a fatal complication of pregnancy. There were 12 cases in which this disease was the primary cause of death during 1941: in 7, the infection followed normal delivery; in 3, the patients died undelivered; and in 2, there had been an operative delivery. Autopsies were performed in 5 cases.

Of the 7 associated with normal delivery, the first case was that of a patient who developed pneumonia on the third post-partum day and died three days later. Autopsy revealed a normal pelvis and bronchopneumonia of the influenza type.

The second patient, when five and a half months along in her second pregnancy, developed pneumonia; a spontaneous abortion occurred the day after hospital entry. The infection was due to a Type 22 pneumococcus, and in spite of sulfonamide and serum therapy, death occurred the following day.

The third patient developed a fever thirty-six hours post partum. Blood cultures were negative; the patient was given sulfathiazole and transfused; a clinical diagnosis of pneumonia was made and confirmed at autopsy.

The fourth patient entered the hospital at term with an acute upper respiratory infection. She had a normal, rapid delivery but died on the tenth post-partum day, autopsy proving the cause of death to be bronchopneumonia and pneumococcal septicemia.

The fifth patient, who had had thirteen previous pregnancies, entered the hospital cyanotic and with a pulse rate of 140. Ten hours after entry, she delivered herself of a 2-pound infant, and lived but thirty-four hours post partum. A diagnosis of pneumonia was confirmed at autopsy.

The histories of the last two cases in this group are incomplete. One of them entered the hospital with influenza and died during delivery. The other case was that of a patient delivered at full term of a living child who died a few days after delivery.

Of the 3 cases allocated to pneumonia who died undelivered, the first was that of a patient, five months along in her third pregnancy, who died four hours after admission to the hospital.

The second patient entered the hospital at term with acute bronchopneumonia. She had had a cold for three weeks and died undelivered three days after entry. An autopsy was performed, and death was found to be due to bronchopneumonia.

The third patient was a woman who, in the seventh month of her third pregnancy, had called her physician because of a severe cold of three days' duration. She was sent to the hospital, and a diagnosis of bronchopneumonia made by x-ray study. Death occurred four days after entry, and a living child, weighing 6 pounds, 3 ounces, was delivered by post-mortem cesarean section. The causative organism was a Type 3 pneumococcus.

The remaining 2 cases were patients who were delivered by operative intervention. The first case was handled unintelligently: after a sixty-hour labor and an unsuccessful attempt at high-forceps delivery, a cesarean section was done. Pneumonia developed postoperatively. This, of course, was an unjustifiable death.

The second patient was delivered by low forceps. There is no evidence in the record that pneumonia was present at the time of delivery, but two weeks afterward x-ray films showed a bilateral lobar pneumonia, from which she did not recover.

It is very gratifying that only one of these cases was a postoperative pneumonia and that this was the only case associated with unintelligent obstetrics. Those patients who died undelivered emphasize particularly the seriousness of pneumonia as a complication of pregnancy. It must be borne in mind that a cold may develop into bronchitis and bronchitis into pneumonia, and that during pregnancy the patient with a common cold must be treated more conservatively than she would be if she were not pregnant. The attending physician should be notified immediately, and rest in bed should be ordered. A cold accompanied by a fever

requires medical examination. Although chemotherapy and serum treatment have undoubtedly reduced the mortality from pneumonia, both methods to be successful require early diagnosis. Only closest possible co-operation between the physician and the patient will make the treatment of pneumonia as successful as it should be.

DEATHS

ADAMS — Charles W. Adams, M.D., of Cambridge, died October 20. He was in his sixty-fourth year.

Dr. Adams received his degree from Harvard Medical School in 1905 and was a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

COON — William H. Coon, M.D., of Easton, Connecticut, died October 6. He was in his sixty-eighth year.

Dr. Coon received his degree from Bellevue Hospital Medical College, New York, in 1897. He had served as assistant physician at the Northampton Insane Hospital, as house officer at the Boston City Hospital, as executive officer of the Harvard Infantile Paralysis Commission, and as health commissioner of Bridgeport, Connecticut.

He was a former member of the Massachusetts Medical Society.

His widow, a son and a daughter survive him.

GREENWOOD — Allen Greenwood, M.D., of Boston, died October 23. He was in his seventy-seventh year.

Born in Chelsea, he received his degree from Harvard Medical School in 1889 and served his internship at the Boston City Hospital. Dr. Greenwood was professor of ophthalmology, emeritus, at Tufts College Medical School and lecturer on ophthalmology in the Courses for Graduates, Harvard Medical School. He was affiliated with the Boston City Hospital, the Massachusetts Eye and Ear Infirmary, the Beth Israel Hospital, the New England Hospital for Women and Children, Adams House, the Waltham Hospital, the Milford Hospital and the Framingham Union Hospital.

Dr. Greenwood was a fellow of the Massachusetts Medical Society and the American Medical Association. He held memberships in the American Academy of Ophthalmology and Oto-Laryngology, the American Ophthalmological Society, of which he was a former vice-president, the Association for Research in Ophthalmology, the New England Ophthalmological Society and the American College of Surgeons.

His widow, two daughters and a son survive him.

WALKER — Harry A. Walker, M.D., of Somerville, died October 30. He was in his sixty-second year.

Born in Binghamton, New York, he received his degree from Cornell University Medical College in 1905. He served for four years in New York hospitals before moving to Somerville, where he was a member of the staff of the Somerville Hospital.

Dr. Walker was a fellow of the Massachusetts Medical Society and the American Medical Association. He was a member of the Somerville Medical Society, the Cornell Medical Alumni, and the Cornell Club of New England.

His widow, a son, and two daughters survive him.

WAR ACTIVITIES

SELECTIVE SERVICE

The following announcement by the Massachusetts state director of selective service is of general interest.

* * *

It has been decided by National Headquarters, Selective Service, not to extend the program of physical rehabilitation. Further activity relative to this program has been discontinued so far as the Selective Service System in Massachusetts is concerned. The names of those physicians, dentists and institutions who have signified their willingness to participate in a program of rehabilitation will be kept on file at State Headquarters.

This is not intended to affect or interfere with projects or programs for rehabilitation of Selective Service registrants on the part of groups or organizations not directly connected with Selective Service.

Local-board examining physicians have been asked to exercise discretion in utilizing the services of examining dentists in the physical examination of selectees. Dental diseases or defects are no longer shown as a cause for rejection by local-board examining physicians. Hence the desire to conserve the time and energy of examining dentists who have been so faithful and loyal in their efforts to make a contribution to Selective Service in the field of dentistry. Some local boards have utilized the services of examining dentists in some capacity outside dentistry. This is, of course, permissible and it is not meant that such activities or help is to be dispensed with.

Examining physicians in full co-operation with their local boards are now engaged in reviewing the cover files of all registrants who have been placed in Class IV*F* because of some physical disqualification. They have been called on to exercise sound medical judgment in studying these records so that those registrants who are hopelessly disqualified for all military duty will be kept at home and all others who are qualified for full or limited military duty will be sent to the induction station.

A study of registrants in Class IV*F* because of a mental or nervous disorder is about to be undertaken. It will be confined to groups of ten or fifteen registrants from each of fifteen local boards scattered throughout the State, urban and rural areas included. The purpose of this study is to determine what proportion of the registrants in this group are qualified, under present standards, for full military duty, as well as to discover what number, if any, now disqualified for military duty are fit subjects for psychiatric or other methods of rehabilitation.

Recently, local boards were directed to begin immediate preliminary reclassification of all married men with wives only. This is of immediate and pressing interest to those members of the medical profession who are now in Class III*A* either because of collateral dependents or because they are married and have no children. The demand for medical officers in the armed forces is insistent; it is pressing; it is imperative. Medical men in the two categories named above who have been declared by the Procurement and Assignment Service to be available for military duty should apply at once for a commission through the Medical Officers' Recruiting Board, 319 Longwood Avenue, Boston. There is always a chance of delay in processing the papers. Occasionally x-ray and other studies are necessary. Local boards are no longer permitted to defer the induction of a registrant so that he may apply for or await the processing of an application for a commission. If a medical man has delayed in ap-

plying for a commission and his order of induction has been issued, he may be inducted and have to serve as an enlisted man before the commission catches up with him.

As the need for medical men in the armed services is becoming more generally recognized, there has been a noticeable stiffening in the attitude of Selective Service officials toward members of the medical profession who have been declared available for military duty yet who refrain from taking the necessary steps until it is almost too late. National Headquarters, Selective Service System, in Local Board Release, No. 89, has said, in part:

> In considering the classification of a registrant who is a qualified medical doctor, dentist or doctor of veterinary medicine, the local board may, if it finds such registrant should not be deferred for reasons other than dependency, take into consideration the pay and allowances which such registrant would receive in the event he is commissioned in the armed forces. In practically all instances the pay and allowances of such registrant, if he were commissioned as an officer, would be sufficient to eliminate the question of dependency.

In this connection, it may be said that it is probable that Selective Service will begin inducting men with dependent wives in the very near future, possibly in November or December, 1942.

If a registrant applies for a commission and he is refused, either because he is found physically disqualified or for any other reason, local boards have been asked to consider classifying him in either IV*F* or II*A*. Class IV*F* will be restricted to those registrants whose physical examinations by the Medical Officers' Recruiting Board reveal the presence of a physical defect which would normally cause rejection at the induction station.

Students in accredited medical, dental or veterinary schools may apply for a commission in the Medical Administrative Corps as soon as they have been admitted to the freshman class. Local boards have been asked to consider for occupational classification (Class II*A*) students who are in good standing in a medical, dental or a veterinary school, as well as those who are in an osteopathic school. This is on the theory that such students are in training for an occupation necessary in the national health, safety or interest.

LIEUTENANT COLONEL VICTOR D. WASHBURN, M.C., A.U.S.
State Medical Officer

38 Chauncy Street
Boston

MISCELLANY

PULMONARY TUBERCULOSIS AMONG SPANISH-SPEAKING PEOPLE

To meet the menace of a rise in the tuberculosis death rate due to war conditions, a renewed emphasis must be laid on special problems in the fight to control and ultimately to eradicate the disease. It is timely and pertinent to call attention to certain of these problems in which assistance of the general medical profession is indispensable.

Industrial problems and racial problems stand out clearly against the background of national health, which is threatened by the exigencies of war. A cogent article (Wilson, W. J. Pulmonary tuberculosis among the Mexican population of Weld County, Colorado. Rocky Mountain M. J. **39**:432, 1942) is illustrative of the situation existing in various parts of this country, one which can only be met by concerted action on the part of the medical profession. The problem in Weld County, Colorado, differs in extent but not in kind from countless similar ones that confront physicians throughout the country.

* * *

It is a well-established fact that the incidence of pulmonary tuberculosis varies markedly in different races. Roughly, there appears to be an increase in incidence as the pigmentation of the skin characteristics of the race increases, and also an increase with the magnitude of climate change occurring when the darker-skinned races migrate to colder regions. Thus, a native of the tropics coming to Colorado to live is more liable to contract tuberculosis than a native Coloradoan. Whereas the present death rate for tuberculosis in the United States Registration area is approximately 36 (in 1940) per 100,000 population in Whites, the rate for Negroes is almost three and a half times that number.

The incidence of tuberculosis in the Mexican falls between the rates for Negroes and Whites. However, reported figures have shown fairly wide variations. These variations are to be expected, since the Mexican who was born and raised in the Rio Grande valley and who later moves across the river into the Texas side of the valley has made no change in climate at all, but the Mexican who migrates from Monterey to Colorado has made a very decided change. It is therefore expected that the incidence of tuberculosis among Mexicans coming to Colorado will be greater than that among those stopping in southern Texas, New Mexico and Arizona.

The Weld County study, under the joint sponsorship of the Weld County Tuberculosis and Health Association and the Weld County Health Department and Public Health Laboratories, shows the tuberculosis problem that exists among the several thousand Mexicans residing in this Colorado county. Nearly all of them are occupied in farm work, mainly the planting and harvesting of sugar beets. Over half of them live in "Spanish colonies." Living conditions are quite uniformly substandard and crowded. This undoubtedly contributes in no small measure to the picture presented by this study.

During the thirty-month period from September 1, 1939, to March 1, 1942, a case-finding program was carefully conducted among the Mexican population of Weld County. A total of 1745 persons were tuberculin tested, and all positive reactions followed up with an x-ray examination. Of the reported studies, very few have contained complete follow-ups of all positive reactors. The Weld County study is now complete except for the progress following diagnosis and treatment of all active cases found.

The tests were made, for the most part, in "Spanish colonies" after showing a series of educational films produced by the National Tuberculosis Association. The interest response was very gratifying, and all age groups attended, as is shown in the figures of Table 1. The ages ranged from less than two years to over seventy.

The remainder of the persons included in the study were segregated from the testing programs carried on in the schools of the county, and a few persons who were tested for various reasons. On the whole, the group studied should represent a very nearly accurate cross section of the Mexican population of the county.

Of the 1745 persons tuberculin tested, 745, or 42.7 per cent, had positive reactions. These 745, along with forty other persons from families in which active tuberculosis was found, were given chest x-ray examinations. These forty people had not had previous tests.

In 481 of the chest x-ray films, there was no evidence of tuberculous activity and they were dismissed from further study.

In 304 cases, radiographic evidence ranged from merely suggestive to definite evidence of disease. These were referred to the Chest Clinic of the County Health Department for further study, including physical examination, sputum examinations and cultures. Sixty-one persons were found to have active pulmonary tuberculosis. Of these, 51 had far advanced disease, 4 had moderately advanced disease, 4 had unusual lesions and 2 refused to co-operate.

Based on this study, the incidence of tuberculosis among the Mexican population of Weld County is found to be the staggering figure of 34.17 per 1000 population. — Reprinted, in part, from *Tuberculosis Abstracts*, October, 1942.

NOTE

The Salem Tumor Clinic held a teaching clinic at the Salem Hospital, on Friday, October 30, with Dr. George W. Holmes, professor of radiology at Harvard Medical School, as the speaker. Dr. Holmes spoke on "General Aspects of Irradiation in Carcinomas."

CORRESPONDENCE

CAROTID-SINUS REFLEX

To the Editor: In an article published in the September 24 issue of the *Journal*, entitled "The Significance of the Carotid-Sinus Reflex in Biliary-Tract Disease," by Engel and Engel, the authors offer some interesting observations. However, their conclusion that a hyperactive cardioinhibitory carotid-sinus reflex in cases of biliary-tract disease is due to "sensitized nervous pathways" is not warranted from their limited observations. Do they imply by "sensitized nervous pathways" a lowering of the synaptic resistance in the vagal center, in the ganglia of the heart or in the resistance offered by the myoneural junctions of the vagus? Or, do they mean a hypersensitivity of the vagus nerve? Furthermore, what brings about such a state? Is it due to a chemical substance elaborated by the disease or to some reflex factor that summates with the impulses coming from the carotid-sinus region? In the latter case one should not consider it sensitization, but summation.

From a physiologic viewpoint, coronary disease, meaning not merely coronary sclerosis but also coronary insufficiency, may explain a hyperactive cardioinhibitory carotid-sinus reflex even in the authors' few cases. All physicians are familiar with the anginal syndrome induced by biliary-tract disease in some patients, especially in the older age groups where coronary sclerosis is usually present. The authors themselves observed it in some of their cases. It is also now generally agreed that the anginal syndrome is due to acute coronary insufficiency caused by increased heart activity during effort or excitement, or by reflex angiospasm of the coronary vessels. It can therefore be readily understood how acute biliary-tract disease may produce coronary angiospasm and resultant coronary insufficiency by impulses set up in the interconnecting vagosympathetic system of the abdominal organs and the heart, and thus produce the anginal syndrome and a lowering of the resistance of the myoneural connections and of the ganglionic synapses of the vagus nerve in the heart.

It is interesting to find that all the authors' 18 patients who presented a positive carotid-sinus cardioinhibitory reflex were over forty-one years of age, and most of them over fifty, when coronary sclerosis detectable or not detectable by clinical or laboratory means is to be expected. The potentiality for an acute coronary insufficiency to develop in such cases under any provocative factor is always present.

It would be interesting to learn how many patients less than forty years of age exhibit the anginal syndrome and the hyperactive cardioinhibitory reflex in biliary-tract disease. The fact must be appreciated, however, as I have brought out in my papers to which the authors refer, that the hyperactive cardioinhibitory carotid-sinus reflex often occurs also in the absence of coronary disease, probably owing to a constitutional weakness in the synapses, which lowers their resistance.

The authors are wrong in their implication that I advocate the hyperactive cardioinhibitory carotid-sinus reflex as the sole diagnostic factor in coronary disease. I suggested its use merely as corroborative evidence in patients who present clinical evidence suggestive of the presence of coronary disease. As such it is occasionally of greater value than the electrocardiogram, and is oftener positive.

Those who have had sufficient experience in electrocardiography know full well the limitations of the electrocardiogram as a diagnostic means.

Louis H. Sigler, M.D.
255 Eastern Parkway
Brooklyn

POLITICAL RESPONSIBILITY OF PHYSICIANS

To the Editor: Physicians are not properly represented in the legislative bodies of our cities, states and the Nation. Members of all other occupations, business and professional, are elected to office. Since physicians are not stepchildren they, likewise, should have adequate representation. I have often and in various ways, at Council and district meetings, tried to exhort, enthuse and encourage physicians to make the sacrifice to become candidates for the Legislature. Indeed, at the recent primaries, after having failed to persuade a single physician to become a candidate, I was finally persuaded to seek the nomination in my district. Since compulsory state medicine is a possibility and since other important medical matters are scheduled to appear before the Legislature, Congress and the courts, it has become absolutely necessary that physicians should take part as members of the law-making bodies.

The National Physicians' Committee, whose work and activity were approved on June 9, 1942, by the House of Delegates of the American Medical Association, has exposed the existing conditions of medicine. We pay taxes and do millions of dollars' worth of careful and faithful work for the poor (and even for many who can afford to pay us, and do not), but no one is taking our part; we certainly do not merit the treatment we are receiving from politicians and the public.

Laymen seem to think that they must have lawyers in the law-making bodies. Of course, they are wrong, but it is up to us, who protect their health, to make them pay a little attention to our ideas. When an organization comes annually to the State House and wants to repeal the vaccination law and another wants to prevent us from using animals for experimentation (at one session, this was up for a second hearing), it is high time that we should protect the population and ourselves by having our own representation.

If compulsory state medicine is passed, the politicians will be in control and will order physicians around. The fine relations that exist between patients and physicians will disappear. Progress and advances in medicine will cease, and chaos will arise. Perhaps some physicians will benefit by this for they will work short hours and receive a fair salary.

Compulsory state medicine would take in hospitals, physicians, nurses, pharmacists and everything else that has to do with medicine. This would involve an expenditure of somewhere in the region of $3,500,000,000 to $5,000,000,000 (which would be controlled by politicians). Physicians must take a determined interest in this matter and definitely express an opinion. California has already defeated such a measure — physicians, hospitals, nurses and pharmacists must awake and act, not tomorrow but now.

Since the Massachusetts Medical Society has just started a plan that will eventually, I trust, take care of the complete cost of adequate medical care, there seems to be little excuse for compulsory state medicine. If we, as physicians, take heed at this time and pay attention to the advice of the American Medical Association and of the National Physicians' Committee to take our own part, we can benefit, and any proposed bill to inaugurate compulsory state medicine can be defeated.

HENRY M. LANDESMAN, M.D.

429 Marlborough Street
Boston

DEPRIVATION OF LICENSES

To the Editor: At a meeting of the Board of Registration in Medicine held October 14, the Board voted to revoke the license of Dr. William E. R. Basch, 183 Harvard Avenue, Allston, because of gross professional misconduct in the practice of his profession.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

To the Editor: At a meeting of the Board of Registration in Medicine held October 14, the Board voted to revoke the license of Dr. Earl Gordon Hersey, 12 Faxon Road, Quincy, because of gross professional misconduct in the practice of his profession as shown by his conviction in court.

H. QUIMBY GALLUPE, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

REPORT OF MEETING

WILLIAM HARVEY MEDICAL SOCIETY

The season's first meeting of the William Harvey Medical Society of Tufts College Medical School was held at the Beth Israel Hospital on September 25, with Dr. A. Warren Stearns presiding. The speaker of the evening was Dr. Alan Moritz, professor of legal medicine at the Harvard Medical School, and his subject was "Distinguishing Characteristics of Forensic Pathology."

In contrast to the ordinary hospital postmortem, the medicolegal autopsy is usually of immediate importance to some living being; in fact, it may determine the life or death of such a person. It may also serve to place great financial liability. The hospital postmortem, on the other hand, usually has only educational value. The medicolegal autopsy, furthermore, is frequently contested hotly by one or several "experts," whereas when the hospital pathologist gives his opinion it is usually considered final.

One of the problems of forensic pathology not ordinarily met by the hospital pathologist has to do with identification. Strange as it may seem, there are an astounding number of missing persons at any one time, and the lack of interest on the part of relatives and friends may be a great handicap. Often nothing but a skeleton is found, and even bones of bears and the primates have sometimes been confused with those of human beings. The roentgenologist is often of inestimable value in determining the identity of an unknown skeleton. Often age can be fairly accurately computed from the character of the epiphyses. The height may be estimated by Pearson's formula, even though only the humerus or femur is available. Sex may usually be recognized from the clothing and, failing that, from the character of the pelvis and other bones. The approximate weight of the individual is somewhat more of a problem, but can sometimes be estimated from stature and clothing.

Information regarding the time of death is frequently of inestimable value in ruling out certain persons in a suspected crime. One cannot always accurately determine the exact time of demise, but it is often sufficient to place the time within a few days or even within a certain month. Specimens taken from different areas of injury may confirm the suspicion that the wounds are of different ages, that is, that some were inflicted an appreciable time before death. A botanist may aid by determining how long a plant or bush has been crushed beneath a body, and an entomologist may add some information by judging the age of the eggs of vermin found devouring a body. Either may place time of death within a two-week period and thus incriminate or free a suspected person.

The medicolegal pathologist must develop a suspicious mind and never be satisfied with the plausible cause of death. An example was cited where a man known to have coronary disease was found dead with no evidence of external violence. A complete autopsy, however, revealed a recent large subdural hematoma underlying a bruise of the scalp, which had been covered by his bushy hair. To determine whether or not a death is accidental is often of extreme monetary importance to the relatives of the deceased. There are many places in the body where external violence may be easily missed or where the latent period between injury and death may be long enough to allow healing of the external wound. On the other hand, death from coronary infarct or cerebral accident may be complicated by the finding of signs of external violence that are, in reality, secondary to a fall.

A knowledge of the fundamentals of firearms is almost a prerequisite for a good forensic pathologist, since it is often his duty alone to call attention to some irregularity in the death of a person who has been shot. Such acuity may result in a decision that the shooting was accidental rather than a homicide. The pathologist may be the only one responsible for collecting bullets or other material that may serve to determine the origin of the ammunition and the gun. Ballistics experts are valuable in identifying the gun in question. The character of the combustion residue on the hand or clothing of the deceased may be an important clue in a question of suicide or homicide, and the amount and distribution of powder around the wounds of entrance are of great value.

NOTICES

ANNOUNCEMENT

Dr. William B. Stevens announces the removal of his office to 319 Longwood Avenue, Boston, on November 1.

PSYCHIATRIC CLINIC

On February 26, 1942, the trustees of the Boston Psychoanalytic Institute voted to establish "a psychotherapeutic clinic for ambulatory patients whose problems are related to the present war situation." The clinic was officially opened on October 5 at 82 Marlborough Street and will function as a service to the community. Civilians with neuroses related to the war situation will be treated without charge.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGY

There will be a meeting of the New England Society of Anesthesiology in the White Building of the Massachusetts General Hospital on Tuesday, December 8, at 8:00 p.m. Dr. J. H. Fine, director of anesthesia, Beverly Hospital, Beverly, Massachusetts, will speak on the subject "The Anesthetist and Fluid Balance."

NEW ENGLAND ROENTGEN RAY SOCIETY

A meeting of the New England Roentgen Ray Society will be held in John Ware Hall, Boston Medical Library, on Friday, November 20. Dr. M. C. Sosman will conduct an x-ray conference from 4:30 to 6:00 p.m. At 8:00 p.m., the following program will be presented:

Roentgen Aspects of Certain Diseases of Bone in Children. Dr. E. B. D. Neuhauser.

Eosinophilic Granuloma. Dr. William T. Green.

Pathological Interrelationship of Lipid Disease. Dr. Sidney Farber.

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY

The fall meeting of the New England Oto-Laryngological Society will be held at the Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, on Wednesday, November 18, at 2 p.m.

SOUTH END MEDICAL CLUB

A regular meeting of the South End Medical Club will be held at the headquarters of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, November 17, at twelve noon.

Dr. Reginald Fitz, state chairman of the Procurement and Assignment Service, will be the speaker.

Physicians are cordially invited to attend.

BOSTON SOCIETY OF BIOLOGISTS

There will be a meeting of the Boston Society of Biologists at the Harvard Biological Laboratories, Divinity Avenue, Cambridge, on Wednesday, November 18, at 8 p.m.

Program

Nature and Properties of Gramicidin. Dr. Rene J. Dubos.

Observations on Immunity in Mumps. Dr. John F. Enders.

Slime Molds and the Problem of Morphogenesis. Dr. John T. Bonner. To be read by Dr. William H. Weston, Jr.

(Notices continued on page xii)

The Original Enteric Coated

THESODATE (*Brewer*)

Theobromine Sodium Acetate†

CLINICALLY PROVED*
EFFECTIVELY ENTERIC COATED
DECIDEDLY LESS EXPENSIVE

PROVIDES 24-HOUR PROTECTION

Given 4 times daily, before meals and before retiring.

Thesodate tablets are available on prescription in 7½ grain tablets, with or without Phenobarbital (½ grain), or 3¾ grain tablets, with or without Phenobarbital (¼ grain), 100 in bottle.

*Literature on request.

†Thesodate capsules are available for those patients who may require extra medication.

BREWER AND COMPANY, INC. **Worcester, Mass.**

Pharmaceutical Chemists Since 1852

Military
Malpractice Insurance

for members of

MASSACHUSETTS MEDICAL SOCIETY

$10,000/$30,000 limits **$15.00**

This policy protects against claims made anywhere in the world and commenced while in service or years after the war, provided services were rendered while our policy was in force.

Limited Civilian Practice Included

Crosbie–Macdonald

GEORGE H. CROSBIE EDWARD J. O'NEIL, JR.
ARTHUR H. CROSBIE

79 Milk Street **Boston**

LIBerty 9538

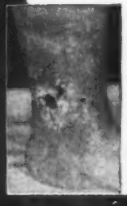
IN VARICOSE ULCERS IT'S
CRURICAST
READY-TO-USE
UNNA'S BOOT BANDAGE
EFFECTIVE and ECONOMICAL

American Medical Ass'n ACCEPTED Council on Physical Therapy

Treat leg diseases the modern, simplified way. Avoid heating, painting, messiness. Save time, gas, and help conserve scarce materials. Get dressing done more quickly.

CRURICAST is always ready to use, easily applied, non-irritating, lightweight, porous, requires no local dressing.

CRURICAST combines support and local dressing in varicose ulcers, and eczema, lymphedema, phlebitis, chronic thrombophlebitic induration. Excellent for partial immobilization.



10 yards long, 3" or 4" wide.

N. E. Distributor
C. H. GOLDTHWAITE CO.
51 Court St., Boston

Made by
E. K. DEMMEL COMPANY
59-11 67th Avenue, Brooklyn, N. Y.

Cook County
Graduate School of Medicine

(In affiliation with COOK COUNTY HOSPITAL)
Incorporated not for profit

Announces Continuous Courses

SURGERY — Two-week intensive course in surgical technic with practice on living tissue, every two weeks throughout the year. General courses one, two, three and six months. Clinical courses. Special courses.

MEDICINE — One-month course in electrocardiography and heart disease, starting the first of every month except December.

FRACTURES AND TRAUMATIC SURGERY — Informal course available every week.

GYNECOLOGY — Informal clinical and diagnostic courses every week.

OBSTETRICS — Informal clinical course every week.

OTOLARYNGOLOGY — Clinical and special courses every week.

OPHTHALMOLOGY — Informal clinical course every week.

ROENTGENOLOGY — Courses in x-ray interpretation, fluoroscopy, deep x-ray therapy every week.

UROLOGY — Two-week course and one-month course available every two weeks.

CYSTOSCOPY — Ten-day practical course every two weeks.

General, Intensive and Special Courses in All Branches of Medicine, Surgery and the Specialties

Teaching Faculty — Attending Staff of Cook County Hospital

Address:
Registrar, 427 South Honore Street, Chicago, Illinois

J. S. WATERMAN & SONS
SINCE 1832
FUNERAL SERVICE
Local and Suburban

Smoking... Nicotine

—and the Strain of **CURRENT LIFE**

A way to encourage patient's cooperation in adjusting smoking hygiene

IN these unsettled times, individuals may tend to display baffling, sub-clinical symptoms. The relationship of these symptoms to smoking and nicotine absorption can be an interesting subject for exploration.*

However, the success of the physician's program is dependent upon the patients' full cooperation.

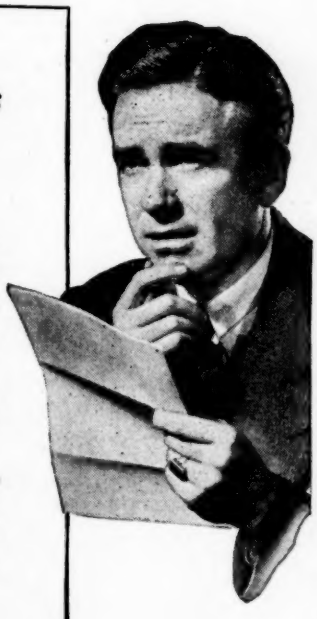
Your recommendation of Camel cigarettes can be an aid in this direction. Millions of smokers favor slow-burning Camels for their extra "pleasure factor"—true mildness, rare flavor.

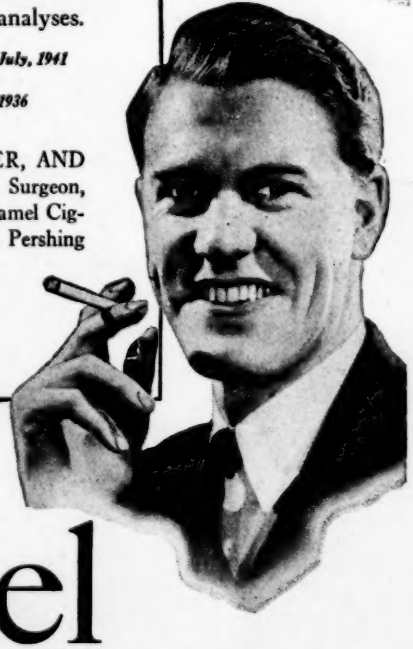
Given adequate support by patients, the physician may find case histories more reliable. In addition, the segregation of such data may facilitate valuable group analyses.

**The Military Surgeon, Vol. 89, No. 1, p. 5, July, 1941*
J. A. M. A., 93:1110—October 12, 1929
Brückner, H.—Die Biochemie des Tabaks, 1936

★ ★

"THE CIGARETTE, THE SOLDIER, AND THE PHYSICIAN," The Military Surgeon, July, 1941. Reprint available. Write Camel Cigarettes, Medical Relations Division, 1 Pershing Square, New York City.





Camel

—the cigarette of Costlier Tobaccos

OFFICE OF CIVILIAN DEFENSE

A course dealing with the medical care of civilian gas casualties is now being presented in the auditorium of Building A, Boston University School of Medicine, 78 East Concord Street, Boston, under the direction of the Office of Civilian Defense. Members of the medical profession are cordially invited to attend the meetings. The first two meetings in this series were held November 3 and 5. The remaining meetings are scheduled as follows:

November 12.

3–4 p.m. Diagnosis and Treatment of Injuries by Vesicants.

4–5 p.m. Tear Gas, Smokes and Systemic Poisons. Decontamination.

November 17.

12:15–1:15 p.m. Gas Masks and Protective Clothing. Treatment of Burns.

NEW YORK TUBERCULOSIS AND HEALTH ASSOCIATION

A scientific session of the Committee on Cardiac Clinics of the New York Tuberculosis and Health Association will be held at the New York Academy of Medicine on Tuesday, December 1, at 8:30 p.m. The subjects to be discussed are as follows: "The Problem of the Cardiac in Industry" and "The Placement of the Cardiac in Industry."

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, November 8

Monday, November 9

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

6:30 p.m. Treatment of Neuropsychiatric Disabilities. Dr. Edward A. Strecker. Massachusetts Psychiatric Society. Hotel Kenmore.

Tuesday, November 10

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

8:00 p.m. New Concepts of Morphine Analgesia. Dr. Donald Slaughter. New England Society of Anesthesiology. White Auditorium of the Massachusetts General Hospital.

Wednesday, November 11

*12:00 m. Clinicopathological conference. Children's Hospital.

Thursday, November 12

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

3:00–5:00 p.m. Medical care of civilian gas casualties. Auditorium of Building A, Boston University School of Medicine.

Friday, November 13

*9:00–10:00 a.m. Selected Problems in Aviation Medicine. Dr. Ross A. McFarland. Joseph H. Pratt Diagnostic Hospital.

Saturday, November 14

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

*Open to the medical profession.

November 17. South End Medical Club. Page xi.

November 17. Medical care of civilian gas casualties. Notice above.

November 17–20. American College of Surgeons. Page ix, issue of August 20.

November 18. New England Oto-Laryngological Society. Page xi.

November 18. Boston Society of Biologists. Page xi.

November 20. New England Roentgen Ray Society. Page xi.

December 1. New York Tuberculosis and Health Association. Notice above.

December 8. New England Society of Anesthesiology. Page xi.

February 13. American Board of Obstetrics and Gynecology. Page 690, issue of October 29.

April 12–16. American College of Physicians. Page x, issue of July 16.

May 18, 19. Massachusetts Medical Society. Springfield.

District Societies

BRISTOL SOUTH

December 3. Fall River.

May 6. New Bedford.

ESSEX NORTH
JANUARY 6.
MAY 5.

ESSEX SOUTH
DECEMBER 2. Salem Hospital.
JANUARY 6. Danvers State Hospital.
FEBRUARY 3. Lynn Hospital.
MARCH 3. Essex Sanatorium.
APRIL 7. Addison Gilbert Hospital, Gloucester.
MAY 5. Salem Country Club.

FRANKLIN
NOVEMBER 10.
JANUARY 12.
MARCH 9.
MAY 11. Annual meeting.
All meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

HAMPSHIRE
JANUARY 6.
MARCH 3.
MAY 5.

MIDDLESEX EAST
NOVEMBER 18.
JANUARY 27.
MARCH 17.
MAY 5.
All meetings are held at the Bear Hill Golf Club, Stoneham, at 12:15 p.m., except that of May 5, which will be held at 6:30 p.m.

MIDDLESEX NORTH
JANUARY 27.
APRIL 28.
JULY 28.

PLYMOUTH
NOVEMBER 19. Plymouth County Hospital.
JANUARY 21. Brockton Hospital.
FEBRUARY 18. Jordan Hospital, Plymouth.
MARCH 18. Goddard Hospital.
APRIL 15. Bridgewater State Farm.
MAY 20. Lakeville.

WORCESTER
NOVEMBER 11. Grafton State Hospital, North Grafton.
DECEMBER 9. Worcester City Hospital, Worcester.
JANUARY 13. St. Vincent Hospital, Worcester.
FEBRUARY 10. Worcester State Hospital, Worcester.
MARCH 10. Memorial Hospital, Worcester.
APRIL 14. Hahnemann Hospital, Worcester.
MAY 12. Annual meeting.

WORCESTER NORTH
JANUARY 27.
APRIL 28.
JULY 28.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Castor Oil and Quinine: Once a doctor, always a doctor. By George W. Vandegrift, M.D. 8°, cloth, 252 pp. New York: E. P. Dutton and Company, Incorporated, 1942. $3.00.

The Surgery of Pancreatic Tumors. By Alexander Brunschwig, M.D., professor of surgery, University of Chicago. Illustrated by Gladys McHugh. 4°, cloth, 421 pp., with 123 illustrations and 1 color plate. St. Louis: The C. V. Mosby Company, 1942. $7.50.

(Books Received continued on page xv)

Industrial Workers with LAME BACK

Often Put Back On Job Quickly

by means of a

SPENCER SUPPORT

Higher morale—greater efficiency—longer hours of work with less fatigue often follow when a worker wears a Spencer Support designed especially for him (or her).

Spencers designed for patients with lame back restore balance — lessen movement of part when desirable—afford protection — support abdomen. Frequently, instantaneous relief is experienced.

Spencer Supports are designed of *non-stretchable fabric.* Spencer designers have *never* used rubber to make a corset fit or as a means of support. All Spencers are light, flexible, easy to slip on and adjust—readily laundered—exceptionally durable. They permit perfect freedom action.

Every Spencer is *guaranteed* never to lose its shape. (Ordinary supports soon stretch out of shape and become useless before worn out.)

For service at patient's home, your office or hospital, look in telephone book under "Spencer Corsetiere" or write to us.

Pictured above—*Spencer Sacro-iliac Support for women. A pad is held snugly against sacrum by means of flat bands that encircle pelvic girdle inside garment and merge outside.*

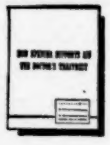
At left—*Spencer Support for Men. Can be slipped on in a jiffy, and adjusted to whatever degree of support is required by means of flat tapes and slides.*

May We Send You Booklet?

SPENCER *INDIVIDUALLY DESIGNED*

Abdominal, Back and Breast Supports

SPENCER, INCORPORATED,
137 Derby Ave., New Haven, Conn.
In Canada: Rock Island, Quebec.
In England: Spencer (Banbury) Ltd., Banbury, Oxon.



Please send me booklet, "How Spencer Supports Aid the Doctor's Treatment."

..... M.D.

Address A-6

63rd Year

RING SANATORIUM AND HOSPITAL

ARLINGTON HEIGHTS, MASS.

For the diagnosis, care and treatment of mental, nervous and chronic medical diseases.

Facilities for all accepted therapeutic measures, including artificial fever and shock therapy.

Outpatient department for referred cases only. Moderate, all-inclusive rates.

VOLTA R. HALL, M.D., MARTHA BRUNNER, M.D.
Resident Physicians

HALLAM T. RING, *Administrator*

163 Hillside Avenue Tel. ARL 0081

Perkins School

LANCASTER, MASS.

Devoted to the scientific understanding and education of children of retarded development.

Five homelike and attractive buildings surrounded by 85 acres of campus and gardens.

Medical Direction *Experienced Staff*

FRANKLIN H. PERKINS, M.D.

Baldpate, Inc.

Georgetown, Mass.

GEO 2131 — Boston Office KEN 8100

For the treatment of psychoneuroses, personality disorders, psychoses, alcoholism and addictions.

Psychotherapy is the basis of treatment; other methods such as *shock therapy, malaria* and *fever box* are used when indicated.

Occupation under a trained therapist, diversions and outdoor activities.

H. C. SOLOMON, M.D., *Psychiatrist*
G. M. SCHLOMER, M.D., *Medical Director*
SELWYN BRODY, M.D., *Resident Physician*
H. JANE MONTZINGO, M.D.,
Resident Physician

Doctors' Stationery

PROFESSIONAL PRINTING

For quotations on your particular requirements send copy to us or

Telephone GARrison 1470

THE A-B-C PRINT SHOP
123 Heath Street, Boston, Mass.

WOODSIDE COTTAGES

Framingham, Mass.

A sanitarium specially adapted for nervous and convalescent patients who need rest and upbuilding in normal surroundings.

No committed mental cases.

ARTHUR H. WARD, M.D., *Medical Director*

Wiswall Sanatorium

203 Grove Street

Wellesley, Mass.

A small group of attractive buildings for the care and treatment of nervous and mild mental diseases.

Facilities for training and diversion under the direction of a competent therapist.

E. H. WISWALL, M.D.
Superintendent

HALE POWERS, M.D.
Resident Physician

Tel. WEL 0261

STAMFORD HALL

Stamford, Conn.

Telephone — 3-1191

Founded in 1891 by the late Amos J. Givens, M.D., LL.D., this sanitarium specializes in the diagnosis, care and professional treatment of nervous and mental diseases, drug and alcoholic addictions and aged folk.

Beautiful location; skilled psychiatrists and large assisting staff.

Located on Connecticut Route 104 near city of Stamford.

Booklet on request.

FRANCIS M. SHOCKLEY, M.D.
Physician in Charge

Dr. Taylor's Private Hospital

For the Treatment of

NERVOUS DISEASES

Alcoholism and Drug Addiction

House well equipped and furnished, skilled attendants, good food and comfortable rooms at moderate rates.

Methods of treatment are those proved best after 30 years' successful experience.

FREDERICK L. TAYLOR, M.D.

45 Centre Street, Boston, Mass.

Near Dudley Street Terminal Roxbury District

Glenside

JAMAICA PLAIN, BOSTON, MASS.

A small, attractively located sanitarium for nervous, mild mental or chronic illnesses.

MABEL D. ORDWAY, M.D.

6 Parley Vale Tel. ARN 0044

WESTWOOD LODGE

Westwood, Mass.

A modern private sanitarium within fifteen miles of Boston, for the treatment of nervous and mild mental diseases; also for those in need of rest under medical supervision. Separate buildings make possible a satisfactory grouping of patients. The buildings, which include one devoted exclusively to occupational therapy, are surrounded by over one hundred acres comprising woodlands, gardens and pine groves.

Superintendent
WILLIAM J. HAMMOND, M.D.
Resident Physicians
SIDNEY M. BUNKER, M.D.
ELSIE S. NEUSTADT, M.D.

A Note Worth Reading

The advertising space in the *Journal* is your guarantee that the products you buy are of the highest quality. Only desirable firms are represented in these pages: they will continue to advertise only if you buy from them and thus prove to them that the *Journal* is the medical authority for reliable advertising.

SPEECH DEFECTS

are usually correctable. All kinds of speech defects are being successfully treated. Individual instruction. Write for descriptive booklet.

S. D. Robbins, INST. FOR SPEECH CORRECTION, Inc.
Formerly Boston Stammerers' Institute — Founded 1867
419 Boylston Street, Boston Tel. KEN 6800